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THE TREATMENT OF ACUTE AND CHRONIC PROTEIN DEFICIENCIES

Collective Review

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In a recent communication (24) the subject of hypoproteinemia was extensively reviewed and discussed. The conclusions arrived at can be summarized as follows:

The role of the proteins or their derivatives (amino acids, peptides, and others) in the human economy is of paramount importance. Besides being the most important structural constituent of all of the body tissues, proteins enter into part or all of the structure of the various enzymes (pepsin, trypsin, and others), hormones (insulin, pituitary and parathyroid hormones, and others), and the various antibodies (modified serumglobulins).

During conditions of health and illness, the protein metabolic function and its daily regulation depends primarily upon good liver function. Normally the plasma protein level of the blood bears an approximately constant relationship to the fixed tissue protein supplies in the body, and both of these are guarded against ordinary and excessive demands by the large hidden reserve supplies of protein in the various organs and tissues of the body.

Protein replacement in general takes place from ingested food. Plasma proteins are renewed constantly from the reserve stores of plasma protein building material as well as from newly ingested amino acids. Not only the quantity, but also the quality of the food proteins is of the utmost importance in the production and regeneration of the various plasma and tissue proteins.

In the light of present evidence it would seem that plasma, tissue, and reserve proteins do not remain static after being elaborated, but rather participate in a dynamic equilibrium as suggested by Madden and Whipple (12), and that the normal balance results from the continuous ebb and flow between the old and the new in the continuation of the normal metabolic activity.

The food supply of protein furnishes the material for the regeneration of all of the protein fractions in the total plasma protein—albumin, globulins, fibrinogen, and prothrombin. After the amino acids (resulting from the hydrolytic digestion of the food protein) reach the liver by the portal vein, they are built partly into proteins and partly into plasma protein-building material. A portion of this synthesized material is placed in the reserve store of proteins. In these reserves are placed the precursors of the plasma proteins, although a portion is stored as fully formed protein, which is then available instantly in times of stress. It is apparent, therefore, that the cycle of plasma protein formation revolves around the liver, both from the viewpoint of formation and from that of storage.

PLASMA PROTEIN DETERMINATIONS

The presence of continued low plasma protein concentrations should be taken as a clinical indication of a profound nutritional disturbance and of a general metabolic deficiency disease. This may be a primary condition, or may be secondary to serious disease, especially of the liver parenchyma. Any manifestation may, therefore, be either the cause or the result of this abnormality, and, commonly, both of these effects become intertwined clinically. Specifically, this has special reference to the albumin and globulin fractions of the total plasma protein in general cases of hypoproteinemia (undernutrition) and to the fibrinogen and prothrombin fractions in sharply defined

activities relating to the blood clotting materials and function.

The importance of plasma protein estimations for clinical purposes lies in the fact that they can be measured. In making these determinations, however, one must take account of any accompanying state of dehydration or hemoconcentration as this tends to give abnormally high values, or of any state of excessive blood hydration which would decrease the relative total serum protein content. Estimations of the total plasma protein concentration in the blood may not indicate the true status inasmuch as a diminution of the serum albumin fraction may coexist with a corresponding increase of the serum globulin fraction. For this reason, blood-volume and albumin-globulin-partition studies are necessary in each case because the total plasma protein contents may not be correctly indicated by the concentration per unit measure of blood. In any event, plasma changes are clinically demonstrable only when the reserve supplies of protein are sufficiently compromised. In general, the amino-acid content of the tissues is about ten times as great as that of the blood plasma. We do not have accurate knowledge of what proportion the hidden reserves of protein-building material bear to either one of the latter. But it must be very large indeed, because changes in total serum protein do not occur until the body weight is appreciably compromised, except after severe hemorrhage, traumatic shock, burns, and so on.

In clinical practice, a single determination is not of much value. However, a succession of repeated observations is immensely valuable because it reveals the course of the disturbance through the deterioration or improvement, primarily, of the protein function and, secondarily, of any liver cell damage. When repeated in a series, quantitative estimations of any protein deficiencies, and their progression or retrogression, give valuable information concerning the state of function of the liver parenchymal cell, or of the deficiency in general, and enable fairly accurate prognostications. So that when the deterioration of function, as indicated by the repeated tests, indicates a progressive diminution, or when the grade of deficiency is very extreme, these laboratory determinations act as important criteria for determining the immediate advisability of any contemplated operation, the choice of an anesthetic, or the method of operative procedure. In some cases, they suggest efforts to improve the disabling factor and operation must then be postponed until the disability is removed or sufficiently improved. In still other cases, they establish the irreversibility of the already existing damage, and, when this is sufficiently far advanced, they contraindicate conclusively any operation of an elective nature.

In a general way, the laboratory demonstration of hypoproteinemic states with or without a coincident loss of body weight, indicates some interference with liver cell function. But inasmuch as the method of production of this deficiency varies, there can be no assumption of intrinsic liver disease, except as it corroborates one's diagnosis on other more appropriate and reliable criteria. Nevertheless, even for this purpose, repeated determinations are valuable as corroborating proofs of liver cell damage, when all other clinical and laboratory findings point definitely to the liver as the essential seat of the disease, and, to a lesser extent, when latent disease is suspected.

CLASSIFICATION OF HYPOPROTEINEMIAS

In accordance with the basic production mechanism of hypoproteinemia, one can distinguish three types (Davis and Getzoff, 5) of this general protein deficiency:

1. Hypoproteinemia of the prehepatic type, which is caused by interference with adequate nutrition intake, digestion, or absorption of plasma protein-building materials, without any disturbance of the ability of the liver to form plasma proteins as the supply of protein-building material is inadequate. This is the most general and important cause of hypoproteinemia.

2. Hypoproteinemia of the hepatic type, which results from the inability of the liver itself to build plasma proteins, despite the fact that adequate supplies of plasma protein-building material are received. In most of the reported cases, this is accompanied by other evidences of a reduction of liver function in the presence of apparent liver disease. A similar effect is demonstrable in latent hepatic disease also.

3. In the posthepatic hypoproteinemia, there is an adequate formation of plasma proteins by the liver, but an abnormal amount of plasma proteins is lost; for example, (a) in repeated bouts of, or in a severe, diarrhea; (b) in excessive albuminurias (nephroses); (c) following a large hemorrhage; (d) accompanying any outpouring of serum in any hollow cavity (pleural effusion, peritoneal ascites, or peritonitic exudation); and (e) following the exudation of serum in large traumatic areas (burns). This form is often combined with undernutrition (group 1).

CLINICAL DISTRIBUTION OF HYPOPROTEINEMIA

Various grades of hypoproteinemia have been clinically observed in many abnormal states and

in many forms of disease. In undernourished and otherwise apparently healthy individuals, the protein reserves become dissipated and exist at abnormally low levels without any subjective or objective manifestations. The compensatory mechanism is sufficient to make good the ordinary wear and tear of the tissues up to a certain point, and there may be no laboratory or other method of determining the state of the protein reserves. However, upon the appearance of any undue strain—illness, anesthesia, operation—this deficiency may become clinically perceptible, and frequently be demonstrable by laboratory means it is not already apparent clinically.

Hypoproteinemia of this (prehepatic) type occurs in periods of famine (in India, China), during wars (the first World War), as a consequence of individual whims in dieting (vegetable diets and so on), in alcoholics, often in pregnant women who do not take sufficient nourishment, and both before and after operation in malnourished individuals.

In industrial practice. Fatigue is, probably, the most important form and cause of disability in the industrial worker. It is an important factor because it spells decreased and/or faulty production, either for the individual himself, or, because of his deficiencies, for his fellow workers when he is engaged in team work. Any extraordinary form of fatigue or its undue prolongation should immediately arouse suspicion that some underlying disturbance is present. Two factors operate to bring this situation about: (1) sufficiently severe undernutrition, and (2) any form of latent disease, especially of the liver. Under these conditions a state of protein deficiency and hypoproteinemia results, the symptoms of which include: (1) loss of weight and strength; (2) loss of stamina or "pep"; (3) various degrees of chronic fatigue; (4) a much lessened resistance to other varieties of infections and disease; and (5) deficient healing power in any industrial and/or other trauma. At the same time these symptoms are the earliest manifestations of latent hepatic disease. In many cases all of these factors became involved in a vicious circle and the one aids, abets, and intensifies the others and their effects.

Any industrial worker showing any of these manifestations should immediately be examined for any possible state of protein deficiency or hypoproteinemia, and for the possible presence of any associated latent liver disease.

In military practice. No matter how well soldiers are fed behind the front lines, nutrition is very apt to deteriorate under combat conditions. Frequently the men are under "starvation" conditions. There is decreased general resistance to any extraordinary episode or trauma, and the general condition is not what an active soldier should possess. In previous wars, the healing of wounds was notoriously behind that seen in civil practice. There is loss of weight and protein deficiencies are undoubtedly common. The fact that plasma transfusions have done such wonders for the wounded in this war only goes to show that plasma furnishes much ready protein for the injured soldier. Acute protein deficiencies are a feature of the extensive burns which present battle practice and methods have caused to a much larger extent than any previous war. It is to be remembered how important an enriched protein diet is for all the wounded, otherwise disabled, and convalescing soldiers in all evacuation and home hospitals.

In traumatic conditions. Acute and subacute protein deficiencies occur in association with extensive traumatic conditions, large suppurating wounds, severe infections, and, especially, burns. In the latter the protein deficiency corresponds to the extent of the burned area, and when the latter is large, the protein loss attains extraordinary amounts.

Nutritional edema. Occasionally one sees patients who have general (subcutaneous, serous cavity) edema without evidence of the usual forms of pathology which produce such waterlogging. They have no elicitable manifestations pointing to nephritis, hypertension, cardiac disease, cirrhosis, myxedema, or a malignant growth.

We have come to know that these patients have moderate or excessive degrees of hypoproteinemia, sometimes as low as 4.5 gm. per cent of total serum protein. There is reason to believe that an underlying liver parenchymal disease is present, and they improve when adequate supplies of protein are provided. For want of a better name, their condition has been included under the general term of "nutritional edema."

Starling (20) was the first to call attention to the part played by the osmotic pressure of serum proteins in regulating the interchange of fluid between the blood stream and the tissues.

The Starling hypothesis has helped to explain these clinical conditions. Sufficient available protein helps to maintain a normal colloidal osmotic pressure in the blood stream and in the capillary bed. Protein deficiencies are now thought to disturb the physicochemical conditions to the extent that water is retained in the body tissues with the formation of edematous areas, and in the hollow spaces with the accumulation of effusions. This change causes more or less reduction in the amount of urine secreted, causes states of hemoconcentra-

tion, and facilitates pseudo-obstructive manifestations. Nutritional edema and the otherwise obscure accumulations of fluid in the hollow spaces and cavities are only understood on this basis.

Occasionally similar forms of general edema occur when the total serum protein level is apparently in the normal range. In these seemingly paradoxical cases, it is found that the albumin concentration is low and that the globulin concentrations are increased; that because the osmotic pressure of the globulin fraction is much lower than that of the albumin fraction, there is a lower total osmotic pressure; and that this disturbed physicochemical relationship permits fluid to accumulate in the tissues and hollow spaces.

Hypoproteinemia with other differentiated forms of disease. In clinically established disease, protein deficiency including lessening of the normal reserve occurs in any basic condition of undernourishment (from insufficient diet to actual starvation, in prolonged vomiting, and so on); in any condition associated with loss of digestive capacity (disease of the stomach, pancreas); in any condition associated with decreased intestinal absorption with or without increased alimentary-tract elimination (the various diarrheas and dysenteries).

Hypoproteinemic states are found in all varieties of established or latent liver diseases (atrophic and hypertrophic cirrhosis, the various forms of acute and subacute yellow atrophy, biliary cholelithiasis, acute and chronic cholangitis in gross and capillary forms); after burns of the body; in luetic, tuberculous, and malignant disease of the liver; in all forms of traumatic, toxic, and/or chemical injury of the liver; and in the destruction accompanying liver suppuration (Johansen, 11; Thompson, McQuarrie, and Bell, 21; Casten, Bodenheimer, and Barcham, 3).

In severe thyrotoxic disease, two factors operate to produce protein deficiency: (1) an associated parenchymal lesion in the liver; and (2) the increased catabolism of protein due to the generally increased metabolic activity as shown by the high metabolic rate. The importance of this is becoming more and more generally known.

Protein deficiency also occurs in renal conditions (nephroses) in which albuminuria is an important factor. In certain severe conditions accompanied by excessive loss of nitrogen due to abnormal destruction of tissue, there are large losses of nitrogen in the urinary output, and the tissue and reserve stores of protein become abnormally depleted. Frequently, too, this loss is enhanced by the inability to take and absorb nutrition for replacement purposes. Protein deficiency is also found in the malnutrition accompanying the wasting of any chronic disease (malignancy, tuberculosis), and very often in association with various grades of anemia.[1]

POSTOPERATIVE HYPOPROTEINEMIA

A state of negative nitrogen balance exists for varying periods after operation. The important factors include: (1) anesthesia; (2) a major surgical procedure with operative manipulation of deeply situated viscera and tissues; (3) a brief period of starvation; (4) shock, fever, vomiting, and the presence of injured tissues. In addition, Cuthbertson (4) has demonstrated appreciable losses of nitrogen after severe and extensive operations as well as after severe injuries. There seemed to be no correlation between age, sex, the presence or absence of malignant neoplasm or other type of disease, and the extent of nitrogen loss.

The adverse effect of general and spinal anesthesia upon the liver cell seems to be increased in hypoproteinemic states, and by the preoperative and postoperative use of drugs of the sulfanilamide group, which also have the tendency to increase any destructive effect upon the liver cell.

Various studies have indicated that pulmonary complications occur much more frequently in elderly malnourished subjects than in others. In these persons the usual hypoproteinemias which occur and are expected after severe abdominal operations seem much more increased.

The major portion of the protein loss occurs during the first four or five days after operation during which time food is not permitted at all, or only in limited quantities; and, ordinarily, this seems to be the most important factor. Since this brief period of protein deprivation or limitation is well tolerated, the vast majority of patients recover without any special attention to the temporary abnormality of the nitrogen balance, and the hypoproteinemia is made good directly after the return to full diet. However, the diet must contain not only protein but also carbohydrate and fat, as nitrogen equilibrium cannot ordinarily be achieved on a pure protein diet.

POSTOPERATIVE ASTHENIA

Quite commonly, it has been clinically noted that following major surgical operations of various types, there is frequently a rather prolonged asthenia which is often appreciable for a few

[1]There are certain congenital malfunctions of the protein metabolism in which the disturbance is not reflected or recognized in any demonstrable anatomical pathology. The subjects are in apparent good health and the only evidence of any such disorder is an increased excretion of an abnormal urinary constituent, usually an intermediate product in the metabolism of a particular body substance. These congenital disturbances of the protein metabolism, known clinically as cystinuria, alkaptonuria, phenylketonuria, and tyrosinosis, have no relation essentially to the subject under discussion.

weeks or even longer after discharge from the hospital. Leriche has referred to this syndrome, which cannot be clearly defined, as "maladie postoperatoire," and ascribed it to generalized disturbances of the sympathetic nervous system. This form of asthenia has been encountered, perhaps, most often after operation upon the pancreas—pancreatic asthenia (Whipple, 23)—and less often upon the gall bladder and liver; or after severe destructive disease. Not enough is known concerning all of these forms of postoperative asthenia, and further investigation is necessary. But it is interesting to speculate upon the possible role of any postoperative nitrogen loss in this connection. While the quantity of tissue protein lost may not be large, the source and character of the catabolized protein under these conditions are not known and might conceivably differ from those of the stores depleted. A general hypoproteinemia may result, or there may be a loss of certain reserve protein fractions or of necessary preceding amino acids, when in the course of their usual activities the subjects simply refrain from their customary protein foods, and nevertheless continue their normal activities.

Multiplicity and combinations of causal agents and conditions. In many cases, both surgical and medical, more than one cause for the hypoproteinemia is present. There are often associated anemia and avitaminoses.

The Treatment of Clinical Hypoproteinemia

The preventive treatment of hypoproteinemic states depends to a great degree upon the cause of the deficiency, and upon the method of its production. In ordinary states of undernutrition, the essential of therapy is increased and abundant nourishment. In disease of the gastrointestinal tract, this must be combined with rectification of the underlying disease, either an increase of the digestive action or an elimination of abnormally increased bowel evacuations. In hemorrhage, replacement of the lost blood is imperative. In essential disease and/or injury of the liver parenchyma, removal of the cause (chemical or other poisoning, deficient food with and without deficient vitamin supply) must be accomplished. In thyrotoxic disease, lowering of the basal metabolic rate with drugs (iodine, thiouracil and others) or by subtotal thyroidectomy with or without preceding medication is necessary. In renal nephroses and albuminurias, the kidney condition must be improved, and so on. In mild states of hypoproteinemia, these measures including the proper additional supply of protein foods by mouth will suffice.

In operative cases the assurance of an adequate supply of protein is most important: first, to protect the liver from the possible toxic effects of anesthesia; second, to prevent tissue edema, which interferes with healing of the wound, and, third, to supply the essential nutrients required for tissue repair and regeneration.

The emphasis which has been placed on correcting dehydration and electrolyte losses before and after operation has often been accompanied by failure to consider the mechanism involved in keeping fluids in the blood vessels (Starling hypothesis). Proper control of the fluid and electrolyte balance in surgical patients receiving parenteral fluids is not possible unless the serum-protein concentration is maintained within normal limits.

If no success follows in the mild cases or it follows in insufficient degree, if the grade of the protein deficiency is severe or extreme, or if there is any necessity for urgency in the correction of the hypoproteinemic state, more active measures are necessary, including the parenteral replacement of protein. Parenteral replacement of protein can be accomplished by (1) the transfusion of fresh whole blood; (2) the transfusion of wet or dried human plasma; (3) the reinfusion of human transudate fluid (ascitic and/or pleural); and (4) the use of amino acids.

All of these have their distinct place and field of usefulness in therapy, and each, or a combination of them, should be selected in any individual case in accordance with the purpose to be accomplished. In any case, an estimation of the good effect which is being accomplished can be obtained from a laboratory standpoint by estimations of the total protein content of the blood plasma, and, clinically, by evidences of improvement in the general condition of the patient and of any local (operative, traumatic) condition which is present.

1 and 2. Transfusions of Whole Blood and/or Plasma

In emergency conditions and/or in any immediate postoperative period, transfusions of blood are the most satisfactory method for restoring the protein supply, both because of the ease of introduction and because of the rapidity with which results are obtained. Under nonemergency conditions, and in long-standing conditions in which protein replacement therapy must be carried out continuously and for long periods of time, such transfusions are not practicable, except under unusual conditions, both because the supply of blood is necessarily limited and for reasons of cost. When the need for red cells does not exist, excessive whole-blood transfusion can be dangerous

since it may lead to seriously elevated hematocrit values.

When whole blood is, for any reason, not available, human plasma forms a most excellent substitute and approaches practically completely fresh whole blood, even though at present it suffers from the temporary disadvantages of expense and inadequacy of supply. About 1,000 cc. of plasma are required to raise the protein content of the plasma of the average adult 1 gm. per 100 cc. In severe hypoproteinemia many liters of plasma may be needed. When plasma is given, absorption and synthesis are unnecessary. After liver injuries, burns, and so on, plasma transfusions have proved to be life-saving.

3. THE REINFUSION OF HUMAN TRANSUDATE FLUID

In the hypoproteinemia accompanying the cirrhoses with ascites, or in nutritional edemas, human transudates may be used. Remarkable results have been obtained; the plasma proteins become elevated; great diuresis follows; and the ascitic fluid may not reform for quite a long time.

The available transudates which can be used are those in the abdomen and those in the pleural cavity. The latter are much the richer in protein content, sometimes averaging as much as 4.5 per cent; ascitic fluid usually contains between 1 and 2.5 per cent, occasionally as much as 4 per cent. Ascitic fluid is usually more abundant. The fluid transudate is obtained by tapping under rigid aseptic control. It is possible and even desirable to pool fluids from more than one source, as in the use of blood plasma. No grouping or typing is necessary. Before use each batch of fluid should be tested bacteriologically, and any excess complement can be eliminated by heating the fluid in water, both to a temperature of 56° C. for fifteen minutes.

In nutritional edemas and similar conditions, the use of transudate fluid seems especially applicable. In any large center of population, and in any large hospital environment, there should be numerous opportunities for securing such fluid in relatively large quantities. The fluid is easily manipulated, no tests are necessary, and there is a minimum of danger and little or no reaction.

I know of one case (Simons, 19) in which this method was repeatedly employed for a year or more without temperature or other reaction at any time.

4. THE ADMINISTRATION OF PROPERLY PREPARED AMINO ACIDS (HYDROLYZED CASEIN, AND SO FORTH)

Amino acids can keep the body in nitrogen balance, and are much more economical and more easily obtainable than plasma. Amino acids require no further digestion and are available to the cells immediately after they enter the blood stream.

When protein is eaten it is hydrolyzed into polypeptides and into amino acids of the general formula $R\text{-}CH(NH_2)COOH$, by the proteolytic enzymes, pepsin, trypsin and erepsin. The process is very complex. The final digestion of protein takes place in the small intestine, and the resulting amino acids and small peptides (?) pass into the blood stream and are circulated throughout the body. Various cells in the body then take up the amino acids and peptides for the synthesis of nitrogen-containing products into proteins and protein-building material.

The usual human diet contains varying amounts of protein from animal and vegetable sources. The nutritive value of any of these depends upon its digestibility, its potential amino-acid content, and its content of those individual amino acids (valine and methionine) which have been proved indispensable. The known amino acids are:

A. Essential	B. Nonessential
1. Lysine	1. Glycine
2. Tryptophane	2. Alanine
3. Histidine	3. Serine
4. Phenylalanine	4. Norleucine
5. Leucine	5. Aspartic acid
6. Isoleucine	6. Diodotyrosine
7. Threonine	7. Proline
8. Methionine	8. Hydroxyproline
9. Valine	9. Thyroxine
10. Arginine	10. Tyrosine
	11. Glutamic acid
	12. Cystine (cysteine)

The essential amino acids must be present in the dietary protein to assure normal growth for the animal organism. The "nonessential" amino acids either may not be required by the body at all, or may, more probably, be synthesized by the body from other amino acids (Rose, 17). As yet, however, little is known of the quantitative requirements of individual amino acids or the function of each in the body.

Of the amino acids listed in column A above, all but histidine and arginine have been found necessary for the maintenance of nitrogen balance in normal adult males. A deficiency of even one of the amino acids that are essential for tissue construction limits the value of a protein to the animal body. A number of the proteins occurring in foods are deficient in one or more of the essential amino acids.

For example, diets which consist mostly of milk are insufficient for maintenance, as shown by bed-

side experience in postoperative cases; while gelatin, although rich in glycine (an amino acid that may be synthesized by the body) does not contain tryptophane and valine (essential amino acids), nor tyrosine which is nonessential. The amino acids in fish and meat measure up very favorably with the as yet unknown requirements for normal maintenance and growth. Generally speaking, animal proteins contain all or nearly all of the essential amino acids, but vegetable proteins do not. However, one can obtain similar end-results and effects by supplementing the various vegetable proteins with one another, and with or without the supplementation of an amino-acid mixture until the total amount is adequate. Under such circumstances, animal proteins are not absolutely necessary. Customarily, however, human beings prefer a diet containing a large amount (more than half) of the protein from animal sources. In any case, the plasma proteins can be synthesized only if the body receives the proper mixtures of amino acids.

In any condition in which surgical shock is a factor, amino acids[1] find no place because they are foods and when they are injected into the circulation they are taken up quickly by the body cells and removed from the blood stream. Under such conditions, blood and plasma are preferable, because they stay in the circulating blood and raise the osmotic pressure and the volume of the blood.

The administration of amino acids is especially indicated when the need for replacement protein therapy extends over an appreciable length of time; less frequently as an exclusive means; and very much more frequently as an adjuvant method in addition to the ordinary food intake of the individual. Here the oral administration of amino acids finds its special field.

a. The administration of amino acids by the oral route. It has been shown conclusively that a mixture containing all the essential amino acids can be given orally; that, when so administered, the amino acids are rapidly absorbed from the gastrointestinal tract; that in this manner they may be substituted for food protein; that by this means a patient may be kept in nitrogenous equilibrium; and that no untoward effects occur or follow. If such a mixture is given in relatively large quantities, however, it is sometimes irritating.

b. The administration of amino acids by the intravenous route. The possibility of supplying protein parenterally with amino acids was done experimentally as early as 1913 by Henriques and Andersen (10), and has since been suggested for clinical use by others, particularly by Rose (16) in 1934.

The intravenous administration of amino acids has been employed by Elman (6, 7), Farr and MacFadyen (8), Shohl and associates (18), Whipple and associates (22), by myself, and by others. Theoretically the method is good, but it presents several practical difficulties, not the least of which is the preparation of a standardized hydrolysate which is safe for intravenous use.

The earlier difficulties have largely disappeared with successive improvements in the manufacture of a proper hydrolyzed casein, which so far has been found to be the best source of material. The solubility has increased so that a perfectly clear solution can be administered intravenously with minimum danger of phlebitis when long periods of venoclysis are required. However, this danger in any case is not very great with the dilute (2 per cent) solutions.

The most serious difficulty has proved to be the occurrence of occasional febrile reactions (Shohl, 17; Elman, 6; and others).

Untoward reactions are due to one or more factors connected with the manufacture of the hydrolyzed casein, with its method of solution and preparation for intravenous use, or with the technique, i. e., the rapidity of the administration itself. Nevertheless, the preparations now available have been administered to many patients without untoward effects by myself and by other observers.

In the experience of Brunschwig, Clark, and Corbin (2), minor disturbances were frequent; they included anorexia, mild and occasionally severe nausea and vomiting, and a generalized disagreeable flushing sensation. In the exceptional instances, these were sufficiently pronounced to warrant discontinuation of the injections after one or several attempts.

It would appear that in certain types of acute hepatitis, a sudden flooding of the circulation with amino acids is too great a physiological load for the liver to tolerate. Nevertheless, postmortem studies of 9 patients who received substantial quantities of casein digest during their terminal disease failed to reveal evidence of toxic effects ascribable to the digests.

c. The administration of amino acids into the bone marrow. Solutions of amino acids are found to be equally effective when injected into the bone marrow. This method offers a satisfactory way of achieving parenteral injection when the other routes are inaccessible, impossible, or inadvisable

[1] The expression amino acids will be used here in the sense of a soluble mixture of amino acids and other protein-split products derived from the hydrolytic scission of proteins.

The injection of amino acids into the bone marrow was done intrasternally by Altschuler, Sahyun, Schneider, and Satriano (1) with Turkel needles, and it was found that amino acids may be given by this route as rapidly and in as large an amount as by the intravenous route. The results were no different than those with the other methods, but intrasternal administration was advantageous in patients in whom access to the veins was difficult. The Turkel needles may be left in place for twenty-four hours or longer and repeated injections may be given through them.

General considerations in intravenous and in intrasternal administration of amino acids. In various conditions patients are able to metabolize from 5 to 30 gm. of protein in the form of amino acids[1] per hour. The average patient is able to take up to 15 gm. per hour, and when this is properly given about 95 per cent of it is utilizable. The solution should not be administered any more rapidly than the subject can metabolize it. In order to supply enough carbohydrate simultaneously, it is usual and best to give the amino acids in a 5 per cent solution of glucose, either alone or in saline solution. Glucose is usually metabolized at the rate of 0.84 gm. per hour or kilogram of body weight, according to most authorities. Usually large quantities of both amino acids and glucose are required if any good is to be accomplished.

When the paradoxical observation is made that protein concentration is decreasing while the hemoglobin is increasing as fluids are given intravenously, one should deduce that plasma is being lost from the blood stream. According to Minot and Blalock (15), the indication, then, is to give increasing amounts of protein, possibly with colloids to increase the osmotic pressure. Very large amounts are needed.

d. Administration of amino acids by the subcutaneous route. When intravenous amino acid is not well tolerated, a 3.3 per cent solution in distilled water may be given safely by hypodermoclysis without discomfort and reaction in the tissues. Patients with clinical icterus, or nonicteric forms of marked liver damage, as shown by functional tests, commonly have reactions after intravenous injection, but they tolerate hypodermoclyses of the 3.3 per cent solution well.

e. The administration of amino acids by rectum. This has been reported by Griesbach (8), and by McClendon, Cavett and Johnson (13). However, the usefulness of the method is questioned by McLester (14) on the ground that rectal feeding is, at best, limited because of the variabilities of its absorption. I am inclined to agree with the latter statement.

[1]One gram N equals 6.25 gm. protein.

THE MANAGEMENT OF PROTEIN REPLACEMENT THERAPY

a. General considerations.

In a few of the cases with chronic protein deficiency, it may be found possible to provide an adequate diet which will give not only enough calories, vitamins, minerals, and protein, but an excess of protein to correct any existing protein deficiency. However, the correction by such methods requires considerable time. This method will find its greatest usefulness in the mildest type of case, in the postoperative period in subnormal subjects, and possibly in the cases of postoperative asthenia.

However, even in these cases and certainly in all other cases, it is very advisable to reinforce the high-protein diet with amino acids in order to give a maximum amount of protein-building substances. In any case, enough should be provided, if possible, to give a superabundance and this should be supplemented with sufficient carbohydrates and fat.

It usually is possible to feed enough carbohydrates and fat to meet the caloric requirements, and then provide excess protein nutrition by supplementing such proteins as the patient can eat with sufficient quantities of amino acids administered orally.

The amount of protein (including amino acids) administered should be estimated upon the basis of the difference between the nitrogen intake and output of the individual. The amount of total circulating protein is calculated by multiplying the plasma volume by the protein concentration. The amount of other body protein (tissue and reserve protein) is usually estimated to be 30 times the plasma protein. The total nitrogen excretion per day in urine plus feces multiplied by 6.25 will give approximately the amount of protein broken down in the body during the twenty-four hour period.

An intake of protein or amino acids equivalent to the protein destroyed in the body will suffice to keep the body in nitrogen balance, but it will not allow for correction of the tissue protein deficiency or for the raising of the plasma protein level. An additional amount over that required for balance must be given if protein deficiency is to be corrected. Probably the greater the excess, the more rapidly and more efficiently the correction of the deficiency takes place.

The number of calories any one person requires for twenty-four hours for various activities can be

CHART I.—THE FOOD, MINERAL, AND VITAMIN REQUIREMENTS OF AN INDIVIDUAL

(This chart is taken from the recommendations of the Committee on Foods and Nutrition of the National Research Council.)

	Calories	Total Calories Daily Derived from		Calcium gm.	Iron mgm.	Vitamin A+ I.U.	Thiamin§ mgm.	Ascorbic Acid§ mgm.	Riboflavin mgm.	Niacin mgm.	Vitamin D I.U.
		Protein	Carbohydrate and Fat								
Man (70 kgm.)											
Fairly active	3000	280 (70 gm.)	2,720	0.8	12	5000	1.8	75	2.7	18	**
Very active	4500	280 (70 gm.)	4,220				2.3		3.3	23	
Sedentary	2500	280 (70 gm.)	2,220				1.5		2.2	15	
Woman (56 kgm.)											
Fairly active	2500	240 (60 gm.)	2,260	0.8	12	5000	1.5	70	2.2	15	**
Very active	3000	240 (60 gm.)	2,760				1.8		2.7	18	
Sedentary	2100	240 (60 gm.)	1,860				1.2		1.8	12	
Pregnancy (Latter half)	2500	340 (85 gm.)	2,160	1.5	15	6000	1.8	100	2.5	18	400–800
Lactation	3000	400 (100 gm.)	2,600	2.0		8000	2.3	150	3.0	23	400–800
Children to 12 years											
Under 1 year‡	100*	12–16 3–4 gm.*	84*	1.0	6	1500	0.4	30	0.6	4	400–800
1 to 3 years	1200	160 (40 gm.)	1,040	1.0	7	2000	0.6	35	0.9	6	
4 to 6 years#	1600	200 (50 gm.)	1,400	1.0	8	2500	0.8	50	1.2	8	
7 to 9 years	2000	240 (60 gm.)	1,760	1.0	10	3500	1.0	60	1.5	10	**
10 to 12 years	2500	280 (70 gm.)	2,220	1.2	12	4500	1.2	75	1.8	12	
Girls 13–15 years	2800	320 (80 gm.)	2,480	1.3	15	5000	1.4	80	2.0	14	**
16–20 years	2400	300 (75 gm.)	2,100	1.0	15	5000	1.2	80	1.8	12	
Boys 13–15 years	3200	340 (85 gm.)	2,860	1.4	15	5000	1.6	90	2.4	16	**
16–20 years	3800	400 (100 gm.)	3,400	1.4	15	6000	2.0	100	3.0	20	

*Per Kg.

§1 mgm. Thiamin=333 I. U.; 1 mgm. ascorbic acid=20 I.U. (1 I. U.=1 U. S. P. unit).

+Less may be required if provided as vitamin A; greater if chiefly as provitamin carotene.

‡Infant needs increase from month to month. Amounts given are for approximately 16–18 months.

Amounts of protein and calcium needed are less if from breast milk.

**Vitamin D no doubt necessary for older children and adults. If not available from sunshine, should be provided probably up to minimal amounts recommended for infants.

#Allowances based on middle age for each group (as 2, 5, 8, etc.) and for moderate activity.

A good formula for the average grown adult would include carbohydrate from 60 to 80 per cent, fat from 5 to 10 per cent, and protein from 20 to 30 per cent plus the necessary vitamins and minerals.

determined with great precision. For a moderately active person, 45 calories per kilogram are adequate; for a very active worker, 65 calories, and for a sedentary worker, 37 calories per kilogram. Soldiers require from 60 to 65 calories. For an active child, the caloric requirement is quite high, and exceeds that of an adult.

The daily protein recommendation for an adult is 1 gm. per kilogram of body weight, i. e., roughly speaking, 70 gm. of protein a day for the average man with a body weight of 70 kgm., or 10 per cent of the required 3,000 calories. For children under six years of age, 3 gm. of protein daily per kilogram of body weight are necessary. Children above the age of six should be maintained on 2.5 gm. daily per kilogram of body weight until they become adults. Nutritionists, today, are generally agreed that the liberal use of protein in the diet (from 80 to 100 gm., or more, daily) has no deleterious effect either on the kidneys or on the vascular system. On the contrary, there is evidence that a high protein diet stimulates vigor and physiological efficiency.

Amino-acids therapy, to be effective, must be supplemented with sufficient carbohydrates, fats, minerals, and vitamins, and an abundance of fluid to meet the caloric and all other requirements of the body. Under such conditions, amino acids are free to be manufactured into body proteins. They will do this more effectively if protein food substances are supplied in the diet in addition.

b. Protein replacement therapy under specific conditions.

With all of these facts in mind, and under proper laboratory estimations of the protein nitrogen balance of the individual, the following rules can be advantageously used under various conditions. As can be seen, the suggestions follow along in the order of intensity of the hypoproteinemia and general protein deficiency. They should be varied as the indication is acute and demands urgency in treatment, as the therapy is necessary to correct a long drawn-out condition as a result of which a chronic hypoproteinemic state has resulted, or as the indication arises and either disappears or becomes intensified. It should be understood that

each case is a feeding problem in itself and that the latter gains or loses in importance in accordance with the urgency produced by an advanced state of protein deficiency incident to undernourishment, starvation, or severe gastrointestinal disease; by an underlying severe hepatic parenchymatous disease with its resultant nutritional metabolic disturbance; or by some extraordinary circumstance, as an operation.

In calculating the daily necessary amount of protein, the following factors must be considered: (1) the patient's nitrogen balance; (2) the estimated degree of deficiency in the tissue and reserve protein; and (3) the possible continuance of the original disability which caused the deficiency if one exists; finally, an additional amount of protein should be given to allow for any unavoidable error in the computation.

In severe cases one may follow the same rule of thumb that one frequently does with abdominal drainage—whenever in doubt, give more—and in very severe cases one should give as much as possible by every available channel and method up to the limit of tolerance.

In the following conditions, an estimation is made of the daily necessary supply of protein:

In general malnutrition. In early cases of general malnutrition about 2 to 3 times the normal requirement, calculated at the level of 60 calories per kilogram of body weight, should be given. The amount should be increased in accordance with the degree of malnutrition; and in advanced stages as much as the patient will tolerate should be given regardless of the calculated estimate.

In anemia. In advanced cases, as much as 25 per cent of the globin protein may be lost. The serum albumin factor seems to be the necessary replacement item. The fact that an anemia is present indicates that the preceding nutritional disturbance has existed for a long time. Hence it is necessary to follow the same rules as in any moderate or advanced case of general malnutrition.

In nephritis and/or nephrosis. The albumin lost daily in the urine is easily calculated. Anywhere from 2 to 3 times the amount lost is necessary to replace the latter and to make good the other factors previously indicated.

In infections. Metabolic activity is so greatly increased during these infections that from 2 to 3 times the normal amount is necessary.

In burns. Losses of one-third or more of the plasma are often dissipated daily in very extensive burns. These losses are increased with any added infection or in the presence of high fever. The total catabolic loss may be as high as 250 gm. per day plus the amount lost by seepage in the burned area. All of these factors are to be taken into account in estimating the necessary replacement supply of protein. But for practical purposes the maximal amount of replacement therapy (anything up to 10 times the normal requirement or the limit of toleration) should be employed and sometimes the amount needed is more than the subject can assimilate.

In alcoholism and in hepatic parenchymatous disease. Both of these can be considered together because the protein replacement therapy for chronic alcoholism is the same as for the prevention of, or the early-stage treatment for, parenchymatous disease of the liver.

In all stages the essential disability is that of a severe malnutrition. In moderately advanced and in far advanced conditions, the calculation should include the daily loss of nitrogen, an estimate of the tissue and reserve protein deficiency, and a calculation of the amount of protein lost in digestion from the amount administered. Then this should be multiplied several times in order to obtain an exceptionally rich protein diet. In severe cases as much as from 4 to 5 times the calculated normal must be given for a long time before any beneficial result is seen.

In hyperthyroidism. The calculation should include the loss from the extraordinary metabolism due to the disease, plus the deficiency incident to any hepatic parenchymatous disease which is a common complication. The treatment should follow the suggestions given for severe malnutrition plus those for hepatic parenchymatous disease. The nitrogen balance is most important in the calculation; but due consideration should be given to the metabolic rate.

In the preoperative preparation of patients with malnutrition and hypoproteinemia. There is here the double nutritional disturbance resulting from (1) the indication for operation (gastrointestinal disease with either vomiting and/or diarrhea, carcinoma, dysenteries, hyperthyroidism, hepatic disease, and so on), and (2) the operation itself.

All grades of malnutrition will be present, but as a general rule it is well to add together the protein loss present, and to be anticipated in the postoperative period, plus an added increment for good measure. If the time available for this preparation is limited, the most strenuous methods (blood, plasma, and/or albumin transfusion) should be employed, and the amounts given should be increased.

In the postoperative period. For those patients whose operations are necessitated by conditions unassociated with protein deficiencies, no particu-

lar protein replacement should be done as these subjects accumulate and replace any lost protein as soon as they are back on a normal, or somewhat richer normal diet.

In all other patients, in accordance with the degree of the deficiency, the length of time it has existed, the nature of the operation, and so on, the deficiency should be calculated and replaced as in the preoperative preparation, of which the postoperative therapy is only a continuation, with some intensification of the program.

In industrial practice. Physicians should give adequate information to workers on the importance of a rich protein diet for the various reasons outlined in this communication. Emphasis should be placed upon this again and again in order to have this register adequately in the workers' minds. It might be well to distribute pamphlets containing all of this information with specific directions as to diet fractions, and so forth, and how to secure and prepare diets with abundant and palatable protein. As a general rule, if the usual protein quantity be doubled in an otherwise apparently healthy individual, the diet will be protein rich enough for all practical purposes.

Information should also be distributed by lectures and pamphlets as to the relationship of deficient protein to undue fatigue and to latent or apparent liver parenchymal disease. The workers should be warned and encouraged to report to the company physicians if any of these symptoms appear so that the appropriate tests can be made and measures instituted for the correction of any protein deficiency. Diets should have the guidance of nitrogen balance studies. Under any such conditions, however, a diet as rich in protein as the patient can take, according to the directions hereinafter given for malnutrition and hepatic disease, should be prescribed. Whenever indicated by study of the patient, the diets should be fortified with amino acids; and in emergency conditions other methods of administration besides the oral should be freely employed.

In military front-line conditions. Soldiers have always been provided with portable and emergency extra rations in which carbohydrate was the main ingredient on the theory that carbohydrate was what the soldier needed most, and because of its quick utilization and effect. It appears from the newer knowledge that while carbohydrate is truly valuable, protein is much more valuable because of its increased and more prolonged effect and from the standpoint of guarding the individual against infection in wounds, increasing his healing abilities, giving a greater sense of well being, and preventing or neutralizing fatigue.

Under such conditions it seems better to enrich the protein content of these rations to at least a 50 per cent increase. Under any battle conditions the protein content of the soldier's diet should be the richest which can be provided.

Methods and rules of administering protein therapy in pathological states in practice.

1. Increase the dietary protein intake to between 150 and 180 gm. per day. Usually the patient will not or cannot take more by mouth.

2. Use gastric intubation, if possible. This may add as much as 50 per cent to the dietary intake. However, if too much is given, the subjects become distended, develop diarrhea, and much protein is lost.

If, because of a digestive or other disability, the amount of protein taken is not sufficient, the discrepancy should be made good by adding a sufficient quantity of amino acids dissolved or mixed with the food. This is easily done in feeding by mouth and even more easily accomplished by intubation.

3. Give protein by the intravenous route.

a. Transudate (pleural or ascitic) fluid. The protein concentration will vary between 2 and 4 per cent. Usually great bulk must be given to make up for the lack of concentration. It is, perhaps, best to give a moderate quantity at the first administration (250 cc.) as a test for any possible untoward reaction. If any reaction takes place, it might be advisable to use fluid from another donor source. Thereafter, if enough transudate fluid is available, one can give as much as 500 cc. every other day in moderately severe deficiency conditions, and in exceptional cases this amount may be given every day. More than the usual care is necessary to ensure sterility; otherwise reactions are more common than in other transfusions, especially if any source of infection is present.

A coagulum frequently forms in the pleural transudate. This should be filtered out through eight or ten thicknesses of gauze, and at the same time the fluid will be cleared of any cellular content. The protein lost in the coagulum is very small—frequently only ¼ per cent, or less, of the total contained in the transudate. The transudate fluid should be kept warm (not over 56 degrees) during the transfusion.

The use of transudate fluid will find its best place in the replacement therapy of nutritional edema.

Transudate fluid should be an important source of protein for replacement in chronic protein deficiencies. Possibly when it is furnished commercially, methods of collection, processing, and preparation will be better than those used at

present, and reactions will be eliminated or much lessened.

b. Plasma. One may increase the protein concentration by adding dried plasma from one bottle to freshly dissolved plasma in the usual concentration. As high as a 10-to-12 per cent concentration may be obtained in this way.

Plasma is most valuable in the immediate period after severe and extensive burns. As much as from 4,000 to 5,000 cc. must be given each twenty-four hours in order to replace the enormous protein loss through the burned area.

c. Whole blood. This furnishes more protein than transudate fluid or plasma, but the evidence is not sufficient that blood can be used as a source for the protein needs of the organism; 1,000 cc. of whole blood equal 35 gm. of plasma protein and 70 gm. of globin and erythrocyte protein.

d. Amino acids. The solution should be nontoxic, nonantigenic, and biologically adequate. In intravenous use the limiting factor is the amount of vascular sclerosis which might follow. This can be avoided by use of the subcutaneous or intrasternal routes.

A good formula for the parenteral solution is the following:

Amino-acids	30 gm.
Solu-B	1 ampoule
Glucose (5 per cent) in normal saline solution	1,000 cc.

A safe rate of speed for the administration is 30 drops to the minute.

Solu-B is a vitamin preparation of special potency for intramuscular or intravenous use. Each ampoule contains the following:

Thiamine hydrochloride	10 mgm.
Riboflavin	10 mgm.
Pyridoxine hydrochloride	5 mgm.
Calcium pantothenate	50 mgm.
Nicotinamide	250 mgm.

Only one ampoule is given in twenty-four hours.

e. Albumin solution (25 per cent). In chronic hypoproteinemias and protein deficiencies, these suggestions should be followed in the order given in accordance with the needs of the given situation. In cases due to injury (burns, and so on), or in those in which surgery is contemplated or has already been done, it will be found necessary to reverse the order, i. e., begin with parenteral methods and proceed as soon as convenient or practical to a combination of parenteral and enteral methods, and, finally, as soon as the patient's digestive powers have returned to the necessary degree, use enteral methods alone.

In chronic hypoproteinemias of long standing, not associated with any form of surgery, it is possible, as Elman (6, 7) has done, to evolve a rough equation according to which the protein needs (protein deficit) can be calculated. However, this has two disadvantages: (1) under the best conditions, the equation is not as accurate as it apparently seems to be, and for safety's sake the calculated amounts should be increased to make up the margin of error; and (2) the underlying disturbance does not respond to correction on any time schedule and continues for an undeterminable period until recovery takes place; therefore it is best not to set any time limit in which the correction is to be made. In some cases, the underlying condition is irreversible and protein replacement therapy must continue indefinitely.

It is better to calculate the daily requirement as follows:

(MED+DL+NUP) × 2 in which
MED = minimum endogenous daily protein need, usually 25 gm.
DL = daily loss of protein determined from N balance
NUP = part of diet protein which is not utilized (estimated)

The factor 2 is arbitarily chosen to make good any error and to furnish the additional protein from which the contemplated gain is to be made in the correction of the protein deficiency. This calculation can be made quite easily, and such amounts permit the subject to regain the normal protein content with a speed that the body can tolerate. In good subjects, the arbitrary factor 2 can be raised to 3 and even 4. The presence of any hepatic parenchymal disease of any grade makes for difficulty because of the inherent inability of the diseased liver to metabolize the administered protein. It is important never to overtax the capabilities of the subject to absorb the given amounts as otherwise the endeavor will be fruitless. Ultimately, the amount of total protein needed to replace and make good any deficiency is relatively and actually very large.

The observations of Hoffman, Meyer, and Kozoll (Preliminary Studies in Amino-Acid Therapy. *Proc. Central Soc. Clin. Res.*, 1944, 17. Seventeenth Annual Meeting, Chicago, Illinois, November 3 and 4, 1944), indicate that after the parenteral administration of amino acids the curve indicates that the amino acids leave the blood almost as fast as they enter, and since little of the amino acids can be accounted for in the urine, they must have been taken up by the tis-

sues. Retention in the plasma after oral administration is only slightly longer.

Reliance on the plasma protein level as a guide for the efficacy of the administered amino-acid supply is fallacious. Clinical hypoproteinemia represents a far more serious deficiency of tissue protein than that indicated in the plasma-protein level. Hypoproteinemia means a loss of tissue protein at least 30 times as great as the plasma-protein deficiency. Such deficiencies cannot be alleviated by isolated or haphazard injections of plasma. From Elman's calculation, an average of about 375 gm. of protein is required each day for ten days to raise a serum-protein level from 5 to 7 gm. per cent. Should this regimen give the desired rise in plasma-protein level, it does not necessarily mean that an equally successful replacement has taken place in the reserves and tissue proteins. Similar conclusions seem in order for other forms of replacement protein therapy.

In long-standing cases of protein deficiency in which the deficiency is great and the daily nitrogen excretion excessively high, parenteral amino-acid therapy is usually insufficient to remedy the deficiency, and plasma and blood transfusion are not feasible because of expense. All parenteral replacement therapy is indicated in acute conditions when the deficiency has occurred suddenly or comparatively quickly. In the long-standing cases most brilliant results appear to be achieved with a long-continued, very high protein diet fortified with large oral doses of amino acids, and interspersed, as the need arises, with blood plasma and/or ascitic or pleural fluid transfusions.

The object to be accomplished in chronic protein deficiencies is the building-up of tissue and reserve protein to something like the normal amount. If the available observations are correct, it seems that much larger nitrogen balances than those previously thought necessary must be established and retained for a much longer period of time, and the extent of the latter is not predictable but a matter of continued observation. The best guide for the success of the replacement therapy is not the proteinemia level but the gain in total body weight.

THE CLINICAL RESPONSE OF HYPOPROTEINEMIC STATES TO REPLACEMENT THERAPY

The response to replacement therapy of any hypoproteinemia will depend to a large extent upon the mechanism of its production. The severe liver damage of the hepatic type renders hypoproteinemia least responsive to treatment. The posthepatic type of hypoproteinemia associated with burns usually responds rapidly to efficient early treatment. The response of the hepatic type depends largely upon the length of time the hypoproteinemia has existed and the amount of irreversible damage that has occurred. The prehepatic type responds to treatment in proportion to the nature of the cause.

The favorable effect of efficient treatment in clinical states of hypoproteinemia depends upon (a) the ability to remove the underlying cause; (b) the ability to rectify any disturbance of liver function; (c) the relative shortness of time for which these two primary factors have existed; and (d) the relative lack of pathological anatomical changes such as edema and tissue protein defects. Good and favorable results of efficient treatment cannot be expected when these factors cannot be eliminated, or when any degree of infection is present and cannot be controlled.

THE EFFECT OF THERAPY

Adequate knowledge has greatly enlarged the sphere of replacement and enrichment protein therapy as a protective effect: (1) for preventing any impairment of the normal functions of the liver; (2) for preventing the deposition of fat in the liver cell; (3) for a powerful lipotropic activity when abnormal amounts of fat have previously been so deposited; (4) for lessening the susceptibility and increasing the resistance to toxic and chemical injuries, to infection (antibody formation), and to other forms of disease; (5) in the treatment of some medical conditions (such as the cirrhoses) in which protein deficiency is both a potential cause of the disease and an important consequence; (6) in the treatment of conditions such as burns, in which there is a sudden depletion of protein stores; (7) in the facilitation of reparative efforts after chemical and/or toxic injury of the liver parenchyma; (8) in the better general preparation of patients for any contemplated operation; (9) for the prevention of potential specific dangers, such as postoperative hemorrhage; (10) in lessening the injurious effect upon the liver cell of drugs of the sulfanilamide group; (11) in lessening the risk of general and spinal anesthesia; and (12) in enhancing the efficiency of healing in operative and other types of wounds.

Several points have resulted from this study which seem to have a profound clinical importance. In view of the present tendency toward "dieting," one should appreciate the fact that this may produce a state of undernutrition, protein deficiency, and hypoproteinemia, the symptoms of which, perhaps little understood until now, include (1) loss of weight and strength, (2) loss of stamina or "pep," (3) various degrees of chronic

fatigue, and (4) a much lessened resistance to disease. In many cases, this latency predisposes to more profound changes, especially in the functions of the liver. And the prevalence of such latent conditions is very little understood at its true clinical importance among the profession.

It seems to be true that fat people are not necessarily "well nourished." In this type of person usually the available protein is relatively overshadowed by the fat content. A surgeon appreciates this because of his experience that such individuals are not good subjects for surgery.

The impression is growing that, clinically, an enriched protein diet is not only advantageous but also very necessary for anyone about to undergo the abnormal physical strain of surgery with its attendant risk of infection, trauma, and so on, and for the prevention of any danger of postoperative hemorrhage. In this regard, the previous belief that a preponderating rich carbohydrate diet was necessary has suffered.

All of these facts have special significance in military and battle conditions and in the convalescing period of any wounded or otherwise injured person. All of these facts have very special importance in industrial practice, as hereinbefore indicated. In the latter, employers and their medical advisers are only just beginning to appreciate the important relation of an adequately rich protein content of the food of the worker to his productive capacity as the former eliminates fatigue and corrects any latent disease, and thus increases the earnings of the worker and the profit of the employer.

Similarly, it seems that if, at any time, there arises the necessity for the administration of any drug which might have a deleterious and/or toxic action upon the liver, one should supply a very rich protein diet, which would have the tendency to forestall such injury.

The relative importance of the protein fractions is only now becoming sufficiently known and understood. The proteins guard the body's ability to replace its losses through ordinary wear and tear as well as through disease and operative procedures, and they increase the readiness of wounds to heal. Dietary protein protects the organism from infection by supplying the material from which antibodies may be fabricated as the consequence of appropriate antigenic stimuli. By virtue of their lipotropic power, they help to restrain any tendency to store abnormal amounts of fat in the various organs, notably in the liver. They furnish the factors which control hemorrhage, and an abundant, rich protein supply gives a sense of well-being and vigor and does away with fatigue.

UNKNOWN FACTORS

There seems to be a great necessity for the study of certain hitherto elusive factors which seemingly have a profound effect. Not always do the available methods of therapy and protein replacement bring about the desired results to our clinical satisfaction. For instance, it frequently happens that either plasma or whole-blood transfusions are given and not much change is apparent; then a transfusion is given from another donor, and the result seems almost miraculous. It must be, therefore, that certain factors which had not been present previously become available and are provided through the agency of the new donor. Not infrequently these effects are seen clinically.

MEMORANDA ON COMMERCIALLY AVAILABLE PROTEIN HYDROLYSATE PRODUCTS

At this writing only three protein hydrolysate preparations are available on the open market. Each of these is listed below with a short statement as to its method of preparation and its use, as well as with some indications of its advantages and disadvantages.

Aminoids. This is the only product of its kind accepted by the Council on Foods and Nutrition of the American Medical Association. It represents the enzymatic digest of a multiple source, yeast, beef, wheat, and milk, to which carbohydrates are added. It is designed exclusively for direct introduction to the gastrointestinal tract either orally or orojejunally. Aminoids contain a mixture of amino acids and peptides which is readily absorbed and assimilated. The added carbohydrates exert a favorable protein-sparing action. The product is marketed in the form of dry granules, is satisfactorily palatable, and, in addition, may be readily incorporated in a variety of vehicles, which favors prolonged acceptability by eliminating monotony. The biological adequacy of the product has been established by a number of animal tests as well as by the results of clinical work in human beings (Beling and Lee, *Arch. Surg.* 1941, 43: 735), and this product has been found satisfactory as an adjuvant nutrient whenever protein deficiencies were suspected or when there was an increased need for protein.

Amigen. This product is a pancreatic hydrolysate of casein. Digested close to the limit of pancreatic proteolysis, it is well suited for parenteral use. Limitations to its use are the need for a comparatively slow rate of administration in order to avoid undesirable reactions. The product has high biological adequacy as attested to by many animal experiments. It is available in flasks in dextrose solution ready for parenteral intro-

duction and is also marketed in the form of a dry powder. The manufacturers also recommend its use orally. There is some question as to its palatability (Peters. *Federation Proc.*, 3: 198), but the manufacturers say "if an individual makes up his mind to take the solution and will drink a concentrated solution rapidly, and follow promptly with a chaser, it can be taken with a minimum of unpleasantness." Orojejunal use of the preparation has been accomplished successfully.

Parenamine. Until recently this product was marketed under the name "Amino Acids." This hydrolysate is available in bottles containing 100 cc. of a 15 per cent solution of amino-acid materials derived from the acid hydrolysis of casein. The hydrolytic products are fortified by the addition of a reasonable quantity of tryptophane. The biological adequacy of the original product was questioned by Madden and his associates. Since then the manufacturers have devised a new method for the preparation of stable dl-tryptophane and this is contained in the new product which is now being distributed for use. The product has been used with success in many clinical conditions. Its parenteral administration must be done cautiously as too rapid a rate will give severe reactions which are attributed to hyperaminoacidemia. This hydrolysate has been recommended also for oral administration, but again the question of palatability enters to a very serious extent. Further, it is uneconomic to purchase material especially processed to be administered parenterally and then use it orally. This, of course, puts the burden of unnecessary expense upon the patient.

In addition to the foregoing, much experimental work is going on with various hydrolysates and other nitrogen-containing preparations. Highly promising results have been obtained by the use of mixtures of crystalline amino acids which seem to be very efficiently utilized and free of many of the adverse effects noted for parenteral hydrolysates in the foregoing. The current scarcity of such materials, however, makes it unlikely that they will be in general use for clinical purposes for some time to come.

Extensive investigative work along lines designed to produce satisfactory protein hydrolysates for oral or parenteral use is being undertaken by a number of pharmaceutical houses.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Muntarbhorn, S.: Cavernous-Sinus Thrombosis Treated with Heparin and Sulfathiazole. *Lancet*, Lond., 1945, 248: 10.

A case of cavernous-sinus thrombosis or bilateral orbital cellulitus was treated with 42 gm. of sulfathiazole given orally at the rate of 1 gm. every four hours and 1 gm. of soluble sulfapyridine given intramuscularly for three days. Heparin was given in an intravenous glucose-saline drip, hourly at first and continuously from the second day onward; in all, 120,000 units were given over five days. The clotting time during this period was 16 in thirty minutes. The patient made an uneventful recovery.

ADRIEN VERBRUGGHEN, M.D.

EYE

Wright, R. E., and Duncan, H. A. G.: The Giant Magnet in Ophthalmic Battle Casualties. *Brit. M. J.*, 1944, 2: 658.

The authors report the case of a land-mine casualty from Normandy who was admitted to No. 4 Canadian General Hospital. One of the wounds was a penetrating injury of the left eyeball. A small foreign body was found to be impacted in the retina about 3 disc diameters down and in front of the disc. The entrance wound was minute, near the limbus toward 9 o'clock. There was hemorrhage of the retina near the track of the missile, but the lens and vitreous were clear. The vision was 20/20. A roentgenograph showed a single minute opacity corresponding in position to the visible foreign body. Operation was performed under novocain infiltration on July 15, 1944, the same day the injury was received. Good rotation was ensured by dividing the mesial rectus. A 3-mm. incision was made in the sclera through a linear diathermy coagulation, between points of fine silk suture. The incision was seen to be about 1 mm. from the foreign body, which was partially hidden by coagulum. Six short applications of the giant magnet with the tip of a beak-shaped terminal on the wound produced no movement. It was considered inadvisable at this time to extract the particle with forceps. The patient was retained for further consideration. The next day the authors were dealing with a minute metallic foreign body in the vitreous of a German prisoner of war by the posterior route and observed a slight rocking of the foreign body at the end of about the tenth short application, as the current went off and on. Thereafter the particle made larger excursions from the center of the vitreous toward the wound and was delivered through the choroid (which had not been incised) at the thirty-fifth application. The immediate postoperative progress in this case was uneventful; the eye remained quiet, the vitreous clear, and the vision 6/6. This experience encouraged the authors to continue with the magnet extraction in the case tried the day before. On July 28 the sclera was exposed down to the previous wound and the curved terminal placed against it toward the side away from the foreign body. The magnet was then used in short bursts of about four seconds (on a few occasions as long as fifteen seconds) for 75 applications. The current was flowing probably for not more than a total of ten minutes. During this time the foreign body was observed to rock in its bed of coagulum, gradually come out of it, and lie across the wound. The magnet was then too hot to manipulate and it was considered that its insulation was in danger. The patient was returned to bed. On August 2, under continuous pentothal anesthesia, the mesial sclera was freely exposed and the internal rectus was divided again to give free access. The sclera suture was removed from the original wound on which the beak-shaped terminal was placed. The wound elevated slightly at the first magnet application, and the particle, smaller in size than the head of a ½ inch pin, came out at the sixth trial without any hemorrhage or discharge of vitreous. The postoperative course was uneventful, the vitreous remained clear, and vision was good (6/9 with lens).

It has long been known that intermittent applications repeated at a number of sittings will succeed in moving a feebly magnetic particle. It may not be generally realized that a small magnetic foreign body or larger feebly magnetic particle may behave as a nonmetallic foreign body for a considerable number of magnet applications and be labelled as such. Moreover, with such particles the magnet test of pain production in a cocainized eye is useless.

There are further lessons to be learned from this case and other recent cases observed:

1. The posterior route is ordinarily best for the removal of foreign bodies in the posterior segment.

2. The shortest route to the exterior is probably always best, provided it does not drag the particle over or through an intraocular part or structure of relatively greater importance than that in which it is lodged.

3. A beak-shaped magnet terminal is almost essential for work well behind the equator; a blunt core-shaped terminal is sometimes dangerous, especially with highly magnetic large bodies, unless they are situated in the anterior segment, since the field is too diffuse to direct the delivery accurately.

4. It is possible that the removal of small metallic intraocular foreign bodies of feeble magnetism (as

in the case of iron compounds) is determined by the patience and perseverance of the operator and the patient, and the life of the magnet and rectifier more often than we have thought heretofore.

5. It is perhaps stating the obvious to say that examination of intraocular foreign bodies lodged superficially in the skin of the face or body, or in the conjunctiva, is desirable in order to determine their composition and magnetism.

6. To those accustomed to the localization of foreign bodies in civil hospitals in peacetime, the slower and less accurate methods necessitated by war conditions constitute a great handicap.

7. The fact that frequent applications of the giant magnet increase the magnetism of feebly magnetic alloys should influence the technique.

8. The application of a surface diathery terminal to the sclera in the neighborhood of a metallic intraocular foreign body is likely to produce an uncontrollable reaction emanating from the foreign body. For this reason and because of the greater difficulty of withdrawing a magnetic particle from a bed of coagulum, it is probably better technique to apply diathermy to the neighborhood of the scleral wound after the foreign body is removed.

9. If prolonged applications of the Army portable giant magnet are required, as in the case described, it is almost essential to place it on an adjustable stand with a tilting top, beside the operating table.

CHARLES BARON, M.D.

Dunnington, J. H., and Sallmann, L. von: Penicillin Therapy in Ophthalmology. *Arch. Ophth.*, Chic., 1944, 32: 353.

Ten clinical cases of eye conditions treated with penicillin are reported, and the difficulty in evaluating the role of penicillin in determining their subsequent course is discussed. The effectiveness of treatment in infections of the lid border and conjunctiva with pyogenic cocci and gonococci seems well established. There are as yet too few cases to permit an adequate opinion regarding many of the deeper infections of the globe. Some of the clinical cases were given simultaneous sulfonamide therapy, and the combination may prove to be more effective.

Experimental work was carried out on rabbits whose lenses were inoculated with the staphylococcus aureus. Iontophoretic application of penicillin, after an interval of six hours, checked the infection in none of the cases. When penicillin was injected into the lens six hours after inoculation the infection was checked in all of the cases, but when twenty-four hours elapsed it was checked in only 2 of 10 cases.

Further experimental work was done by the direct injection of penicillin into the vitreous. Staphylococcus infection in the vitreous was arrested with a single injection of penicillin when administered within twelve hours after inoculation. If a period of twenty-four hours elapsed between the inoculation and the treatment the injection was not successful.

The injection of penicillin into the anterior chamber of the rabbit caused only a transient inflammatory reaction of mild degree, lasting from one to three days, and the authors conclude that this may be an effective method of administering penicillin in the human eye when transcorneal introduction by iontophoresis cannot be used.

WILLIAM A. MANN, M.D.

EAR

Patterson, W. H., and Smith, G. S.: Latent Mastoiditis in Infancy. *Brit. M. J.*, 1944, 2: 659.

In a series of 120 autopsies in infants and young children, pus was found in the mastoid cavities of 71. Although the highest incidence was observed among patients with a clinical history of "diarrhea and vomiting," pus was found almost as often in patients with a wide variety of conditions. Clinical, postmortem, and bacteriological findings suggest that so-called "latent mastoiditis" is not an etiological factor in the diarrhea-and-vomiting syndrome.

CHARLES BARON, M.D.

NOSE AND SINUSES

Whalen, E. J.: Sulfonamide Compounds in the Treatment of Infections of the Nasal Sinuses. *Arch. Otolar*, Chic., 1944, 40: 481.

The sulfonamide compounds, Whalen declares, are not effective as bacteriostatic agents when used on the unbroken surface of the skin or of the mucous membrane. It is for this reason that it seems illogical to use solutions or suspensions of these drugs for local application to the unbroken mucous membrane of the nose with the expectation that disease-producing organisms in the soft tissues will be affected or controlled. The oral or the intravenous administration of these new chemical agents is the only means by which they can be brought in contact with the disease-producing organisms that are lodged in the lining membranes of the nasal sinuses. They must be used early in the acute infection, before the infected area is closed off by thrombosed vessels.

Rhinologists must review their pathology, revise their surgery, and integrate their knowledge of the new chemotherapeutic agents. With proper timing of indicated surgical intervention, co-ordinated with systemic use of the new drugs and the application of selected bacteriostatic substances to the field of surgical operation, sinus infections of many types can be brought quickly under control.

The local use of sulfadiazine, in the concentration of 2.5 per cent in aerosol, was found to be without effect in controlling the progress of nasal sinus disease, either the acute or the chronic type. Wetting agents were used as vehicles to carry the sulfonamide compounds in the belief that their detergent characteristics would aid in the penetration of the ostiums of the sinuses. The experiment was a complete failure. An attempt at forcing the sulfonamide compounds into these cavities by the displacement method of creating a partial vacuum in the sinuses was without success since contrast mediums and other

solutions were found only in small quantities and in a limited number of the sinuses so treated.

The only successful mode of chemotherapy for disease of the nasal sinuses was found to be that of giving full doses of the sulfonamide compounds by mouth. This treatment must be carried on under observation in a hospital where bacteriological studies can be made, the blood level controlled, and the blood picture and renal functions frequently observed. With this treatment, a large number of sinus infections both of an acute and a chronic nature can be brought under control.

NOAH D. FABRICANT, M.D.

NECK

Figi, F. A., Rowland, W. D., and New, G. B.: Cystadenoma of the Larynx; Report of 4 Cases. *Arch. Otolar.*, Chic., 1944, 40: 445.

A cystadenoma may be defined as an adenoma that has undergone cystic degeneration. Adenomas and cystadenomas may originate in any part of the larynx, except possibly the free edges of the vocal cords since these are covered with squamous epithelium and are practically devoid of mucous glands. The most frequent sites of origin are the ventricles, ventricular bands, epiglottis, and subglottic region. The tumor may range from a few millimeters to several centimeters in diameter. The cystic character of the growth may or may not be evident on clinical examination. A single large cyst may be present or the tumor may be multilocular. Commonly the growth is covered with normal-appearing mucous membrane, but in some cases the mucous membrane is thickened and injected. The enlargement may be slightly yellowish in areas or throughout its extent because of the fact that the cystic contents show through.

The treatment of these tumors depends on their situation and size. Readily accessible lesions of limited extent can be removed by indirect or direct laryngoscopy but extensive growths may require laryngofissure. Indirect removal using a curved forceps and electrocoagulation is feasible but is gradually becoming a lost art in the treatment of benign laryngeal neoplasms generally. Direct laryngoscopy, using either the laryngoscope or the suspension apparatus, is preferable in most instances. Suspension laryngoscopy usually is the treatment of choice for the removal of these tumors since it affords a wider field of vision than other methods and permits the surgeon to use both hands, which enables him to carry out limited dissection. If the tumor extends deeply in the region of the ventricle or into the ventricular band, or if it is growing beyond the larynx, thyrotomy probably will be necessary.

Unless the tumor is obviously benign and well localized and its limits are definitely evident on direct examination, biopsy should be performed before treatment is instituted. The picture presented by a cystadenoma of the larynx may be closely simulated by a malignant tumor developing in the ventricle.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

German, W. J., Brody, ... S., and Harvey, S. C.: Compound Craniocerebral Injuries. *Surgery*, 1944, 16: 874.

A review of the treatment of compound craniocerebral injuries is made, and a comparison of earlier methods of treatment and results with those of the present day is made. A series of 64 cases of compound craniocerebral injuries was treated at the New Haven Hospital, New Haven, Connecticut. The early treatment of such wounds is emphasized as important in avoiding infection and the complications which result therefrom.

The general policy of treatment, as outlined, included: (1) immediate treatment of shock, if present, (2) inspection, not palpation, of the wound; (3) roentgenography to determine the extent of fracture, especially the depression or the sinus involvement; and (4) operation within six hours in all patients surviving the preparatory period. Local anesthesia was the anesthetic of choice.

The surgical procedure followed in this series, and recommended by the authors, included: (1) thorough débridement of the scalp, cranial wound, and devitalized brain tissue; (2) removal of indriven bone fragments and foreign bodies; (3) closure of the dura with silk, if possible; (4) closure of the scalp in two layers with silk; and (5) drainage of the frontal sinus, and of most wounds, for culture. The bone removal was usually en bloc for the comminuted and depressed fractures unless the frontal or sagittal sinuses were found to be involved, in which case fragments were removed.

The mortality rate in this series showed a marked increase with the advancing age of the patients. All patients in the seventh and eighth decades succumbed.

Of 51 patients who lived more than six days 20 per cent had postoperative infection. The total mortality in the series of 64 patients was 26.5 per cent.

HOWARD A. BROWN, M.D.

Lanigan, J. P.: Traumatic Subdural Effusion in Children. *Lancet*, Lond., 1944, 2: 686.

Three cases of subdural effusion in children are reported. The patients gave a history of trauma which had been followed by signs of increased intracranial pressure and a localizing condition indicative of a gross lesion. At operation, a quantity of clear fluid was encountered beneath the dura, and upon release the brain resumed pulsation and gradually began to come up to the dural level. Improvement was very prompt from the standpoint of consciousness and decrease in the motor disturbances.

Operation consisted of exposure through a trephine opening, which was slightly enlarged for purposes of vision.

HOWARD A. BROWN, M.D.

Meacham, W. F., Smith, E., and Pilcher, C.: Chemotherapy of Intracranial Infections; The Treatment of Staphylococcic and Pneumococcic Meningitis with Sulfathiazole and Sulfadiazine. *War Med.*, Chic., 1944, 6: 378.

The authors have undertaken a series of studies on cranial infections, and the present article, the fifth in the series, concerns the treatment of staphylococcal and pneumococcal meningitis with sulfathiazole and sulfadiazine. The report deals with the results obtained in 116 experiments in which the same types of meningitis were treated by oral administration of sulfathiazole and sulfadiazine, and in 36 experiments in which the intrathecal administration of a suspension of microcrystalline sulfadiazine was employed. Experiments were carried out in groups of 12, half of each group being treated and the other half being kept as untreated controls. The treatment was begun forty-eight hours prior to the cisternal injection of the organisms. The treated animals were given 0.5 gm. of the drug orally every eight hours.

In the first experiments, the staphylococcal meningitis was treated by oral administration of sulfathiazole and there was no significant difference between the treated animals and the controls.

In the next group the meningitis was treated by the oral administration of sulfadiazine, and in this group the mortality was definitely lower. Three groups of 12 dogs were treated by the intracisternal injection of a suspension of microcrystalline sulfadiazine. Following this, no convulsions were seen, but several animals had an extreme transitory opisthotonos immediately following the injection, and at necropsy a thick, pasty layer of the drug was found to extend far forward under the base of the brain.

With regard to pneumococcal meningitis, this was produced in 4 groups of 12 dogs, and these were treated with sulfadiazine and sulfathiazole by mouth. Higher concentrations of sulfadiazine were found in the spinal fluid of these dogs than in those suffering from staphylococcal meningitis. In fact, the percentage of recovery from pneumococcal meningitis was proportional to the concentration of sulfadiazine in the cerebrospinal fluid.

From these studies it is apparent that, in conformance with previous observations, sulfadiazine was present in much higher concentration in the spinal fluid than sulfathiazole after oral administration. The staphylococcal meningitis produced in these experiments was not benefited by the oral use of sulfathiazole. On the other hand, the oral administration of sulfadiazine was distinctly beneficial. Cisternal injections of microcrystalline sulfadiazine were not considered beneficial; in fact, they were believed to be harmful. A high concentration of sulfadiazine in the spinal fluid is essential for recovery from experimental pneumococcic meningitis.

ADRIEN VERBRUGGHEN, M.D.

Collis, J. L.: The Etiology of Cerebral Abscess as a Complication of Thoracic Disease. *J. Thorac. Surg.*, 1944, 13: 445.

The incidence of brain abscesses following infection in the chest cavity, and the route followed by the infection from the thorax to the brain have been somewhat prematurely taken for granted. This study was made for the purpose of clarifying views on these matters. Forty-six cases were collected from the Brompton Hospital, from the Birmingham United Hospital, and from an E. M. S. Chest Center in England, and the first 44 of these were used for compilation of statistical tables.

On reviewing the various tables submitted with regard to certain general factors involved in this type of brain abscess, some of these factors were regarded as of negative value; for instance, the age, the side, and the site of the abscesses, the infecting organism, the number of abscesses found, and the side of the primary condition of the chest were so varied as to indicate nothing in particular. A second group of factors, however, were regarded as significant: namely, the preponderance of these abscesses in the male sex; the special clinical picture of this type of brain abscess; the similarity of the various aspects of the brain abscesses—whether they were secondary to lung abscesses, empyema, or bronchiectasis; the fact that the brain complications might follow disease in the lung or in the pleura; the fact that only chronic disease of the chest caused brain abscesses; the increased danger of this complication following surgical interference; and the absence of abscesses in other parts of the body associated with involvement of the brain.

The author was particularly interested in the manner in which the infection spread from the lung or pleura to the brain. It was first suggested that the connection was due to the passage of septic emboli from the lung to the brain. Although this has been a popular theory, it has never withstood anatomical or experimental criticism. Although it might be true for the pulmonary circulation, it certainly is not true for the pleural circulation, which is involved in cases of empyema. Furthermore, very little cerebral manifestation of septic emboli has been observed clinically in the patient, and the classical picture of cerebral embolus has certainly not been fulfilled.

With the rejection of this theory, the theory of paranasal infection developed, but there were many objections to it, particularly in cases of empyema, which are almost cured at the time that the brain abscess develops and the patient cannot at that time be said to be in a chronic septic state. The spirochetal theory was also examined, but as far as the author is concerned, he was not able to demonstrate spirochetes in the brain of any of his patients in the region of the abscess, but there are many artefacts which will give this false impression. Congenital heart disease such as patent foramen ovale was also investigated, but was not properly connected with this group of cases. It is apparent throughout that the place of empyema in the formation of brain abscess is the stumbling block because the pleura has a different circulation from that of the lung.

In order to obtain information concerning other conditions in which substances pass from the lung to the brain, carcinoma was investigated. Whereas bronchial carcinoma most commonly causes metastases to the brain, carcinoma of the breast is in second place, and the latter, of course, is a chest-wall condition. It appears then that the only vessels which communicate between the lung, the chest wall, and the brain are the bronchial and intercostal veins, which drain into the azygos veins; the spinal veins also drain into the azygos system. These veins are valveless and gravity plays an important part in their flow.

Experiments were continued in which opaque materials were injected into intercostal veins, and it was surprising to find the ease with which the opaque material reached the brain via the inside of the spinal canal. It was attempted to reproduce the disease in cats, but, unfortunately, this was unsuccessful. Experiments of this nature will have to wait until monkeys are available.

In view of this discussion and experimental work, considerable evidence was produced in favor of the fact that infected material is carried from the chest to the brain via the spinal veins.

ADRIEN VERBRUGGHEN, M.D.

Harris, W.: Paroxysmal and Postural Headaches from Intraventricular Cysts and Tumors. *Lancet*, Lond., 1944, 247: 654.

The author points out that cysts of the third and lateral ventricles often produce no physical sign, but may present the so-called classical triad of periodic headaches, vomiting, and papilledema. Such a syndrome would lead one to suspect the possibility of periodic obstruction of the ventricular system. Three cases of this type have been reported.

HOWARD A. BROWN, M.D.

Hammes, E. M., Jr.: The Reaction of the Meninges to Blood. *Arch. Neur. Psychiat.*, Chic., 1944, 52: 505.

Autogenous blood in the subarachnoid space of human patients is not well tolerated by the leptomeninges.

The meningeal reaction to blood is evident within two hours of the hemorrhage and begins as an outpouring of polymorphonuclear leucocytes, followed by the appearance of lymphocytes and large mononuclear phagocytes derived from the mesothelial lining cells of the arachnoid.

This cellular reaction is transient and persists only as long as blood, or products of breakdown of blood, are demonstrable in the subarachnoid space.

Permanent effects occur in the form of patchy fibrosis of the pia-arachnoid, with obliteration of the subarachnoid space. This can be demonstrated only after the blood has been present ten days or longer.

From this study, no conclusion can be drawn as to the effect on this meningeal reaction of drainage

of bloody cerebrospinal fluid by repeated lumbar puncture.

Rupture of an intracranial aneurysm is capable of producing sudden death. The patients rarely, if ever, have an associated intracerebral hemorrhage, although intracerebral bleeding is a very common finding among those who survive the immediate insult only to succumb hours or days later.

An intraventricular hemorrhage sufficient to produce clotted blood in the ventricles will not occur following rupture of an intracranial aneurysm unless there is an associated intracerebral hemorrhage.

SYMPATHETIC NERVES

Smithwick, R. H.: The Surgical Treatment of Hypertension. *N. York State J. M.*, 1944, 44: 2693.

The author discusses some of the problems of choosing the proper cases for lumbodorsal splanchnicectomy. A review of the clinical investigations during the past eleven years is used as a basis for the choice of patients who may be suitable or unsuitable for surgical treatment of this type. The details of the operative procedure have been described elsewhere.

In nearly all of a series of 156 cases, there was a significant and persistent lowering of the diastolic blood pressure following operation. This was associated with favorable changes in the eyegrounds, electrocardiograms, and in cardiac and renal function.

The results have been variously divided into groups, according to the degree of drop in the diastolic pressure. The results in women have been significantly better than in men. The cases have been divided into three types, according to the degree of pulse pressure. Surgical results have been poorest in patients with the highest pulse pressure.

The report is based on 215 patients, of whom 179 are living from one to five years following operation, and of whom all had had diastolic blood-pressure levels between 100 and 170 prior to operation. All patients had been subjected to a detailed study from the standpoint of their cardiac function, renal function, and vascular status as estimated by examination of the fundi. They had also been subjected to postural and cold blood-pressure tests. Their blood-pressure response to sedation should be studied.

The decision as to operative advisability was based upon the evaluation of all these studies. Certain contraindications to surgery have been outlined: (1) patients with congestive heart failure and impaired kidney function, with elevated nonprotein nitrogen, or a reduction in intravenous phenolsulfonphthalein (an output to below 15 per cent in the first fifteen minutes); (2) male patients with resting diastolic levels of 140 or more, unless they have had no cerebral vascular accident and there is no evidence of actual impending cardiac failure or failure of kidney function; (3) women patients with resting diastolic levels of over 140—the same rule applying as to men, except that in the male it is suggested that the phenolsulfonphthalein output must be 20 per cent or more during the first fifteen minutes, while in women, operation may be contemplated if the phenolsulfonphthalein output is as low as 10 per cent or more during the first fifteen minutes.

Other tentative suggestions are made with regard to patients in certain special groups in which a study of the surgical results has indicated a probably poor result.

HOWARD A. BROWN, M.D.

MISCELLANEOUS

Peterson, E. W., Kent, B. S., and Cone W. V.: Intracranial Pressure in the Human Subject at Altitude. *Arch. Neur. Psychiat.*, Chic., 1944, 52: 520.

The authors undertook to study the effects of altitude on the human intracranial pressure in a patient with a large cranial defect. The cranial defect measured 16 by 10 by 2.5 cm., and was perfectly healed and freely mobile under stresses of artificially increased pressure.

The degree of herniation of this defect was measured when the patient, while breathing oxygen, was taken to an altitude of 30,000 feet at the rate of 3,000 feet per minute in a decompression chamber. Readings were taken every 10,000 feet on a specially improvised apparatus. Readings were taken also at 25,000 feet after the subject's mask had been removed for two minutes and twenty seconds. There were no significant changes in the intracranial pressure either while the subject was breathing oxygen at an increased altitude, or while he was in an acutely anoxic state (exposure of two minutes and twenty seconds at an altitude of 25,000 feet).

With a specially constructed plethysmograph carefully fitted to the cranial defect, further observations on the intracranial pressure failed to reveal significant alterations when the subject was breathing oxygen at altitudes of as high as 25,000 feet and when acute anoxia of from sixty to seventy seconds' duration was induced at this altitude. With the same plethysmograph technique of recording changes in intracranial pressure, again no significant alterations were recorded either on ascent or descent when the patient was taken to 15,000 feet and kept at this level without oxygen for twenty minutes. A further ascent to 20,000 feet, where the patient remained for ten minutes without oxygen, likewise failed to cause a significant change in the intracranial pressure as recorded on the plethysmograph.

Direct observations were made on the intracranial pressure by means of lumbar puncture. An intact skull was simulated in this patient by closing the cranial defect with a plaster cast. An ascent to 30,000 feet with the patient breathing oxygen did not cause any increase in the spinal-fluid pressure. As has been observed by others, minute bubbles were noted to be rising in the manometer after an altitude of 20,000 feet had been reached. Removal of the oxygen mask for ten minutes at 20,000 feet, caused an increase of

only 23 mm. of spinal-fluid pressure. This was noted toward the end of the exposure to anoxia, and the administration of oxygen caused no change in this pressure.

It was concluded that all of these approaches to the determination of the intracranial pressure showed that no significant increase in the intracranial pressure of man occurred at high altitude and under conditions either of sudden or of more prolonged anoxia. This is contrary to the conclusions of other workers in the field, and is of importance insofar as it indicates that head-injury casualties may be safely evacuated by air. HENRY A. SHENKIN, M.D.

Peterson, E. W., Bornstein, M. B., and Jasper, H. H.: Cerebrospinal-Fluid Pressure under Conditions Existing at High Altitudes: A Critical Review. *Arch. Neur. Psychiat.*, Chic., 1944, 52: 400.

This is a critical review of the literature based on available reports relating to this subject. High altitudes result in the following changes: reduced barometric pressure, reduced temperature, and reduced tension of oxygen. There is no change in the percentage composition of the atmospheric gases.

From their review the authors conclude that reduced atmospheric pressure has very little influence on the intracranial pressure itself; however, expansion of gas in the bowel at reduced pressure may increase the intracranial pressure secondarily to a rise in venous pressure. Cerebral edema may occur and cause increased intracranial pressure because of anoxia. It has been found that the arterial blood increases because of the anoxia of high altitude and this may be a further factor in increased intracranial pressure in the initial stages. It has been believed that the increase in intracranial pressure, as analyzed by experts in the field, was not of sufficient magnitude to be of clinical significance.

The conclusion reached in this highly critical study is that significant increase of intracranial pressure will not occur in the sick or wounded during transportation by air, provided anoxia is not permitted to occur. ADRIEN VERBRUGGHEN, M.D.

Peacher, W. G., and Robertson, R. C. L.: Neurological Complications Following the Use of Continuous Caudal Anesthesia. *Arch. Neur. Psychiat.*, Chic., 1944, 52: 531.

Two cases of infection complicating the use of continuous caudal analgesia, which resulted in neurological changes, are reported.

The first case was one of immediate bilateral sciatica following forty-eight hours of continuous caudal analgesia. Objectively there was a sacral anesthesia with hypesthesia as high as the second lumbar segment on the right, and as high as the fourth lumbar segment on the left. The cause of this proved to be a localized infection in or about the caudal subarachnoid sac. Culture of fluid aspirated from the caudal canal yielded the hemolytic streptococcus and the staphylococcus albus. Frank pus was obtained on lumbar puncture through the fourth lumbar interspace, a culture of which gave pure staphylococcus albus hemolyticus. No spinal fluid was obtained with this procedure and it could not be determined whether the pus was intra- or extradural. Sulfathiazole (6 gm. daily for two weeks) was given, and the patient improved rapidly. She was asymptomatic and neurologically negative on discharge twenty-four days postpartum, and also on follow-up examination made one and one-half years later.

The second patient had a normal delivery with sixteen and one-half hours of continuous caudal analgesia. Her postpartum course was normal until the ninth day after delivery when she complained of low back pain with bilateral sciatic radiation. There was questionable sensory impairment below the third lumbar segment, and bilateral Kernig and Brudzinski signs were present. There was a daily temperature elevation of 103 degrees. Remission occurred with the use of sulfadiazine, but six weeks postpartum the patient was readmitted to the hospital with a recurrence of symptoms. At this time there were hyperactive reflexes and bilateral Babinski signs, as well as signs of meningeal irritation. The temperature was elevated daily to from 100 to 101°F., and there was a leucocytosis of 14,800. Multiple lumbar punctures indicated the presence of a partial subarachnoid block between the second and the fifth lumbar interspaces, and pantopaque myelography gave the picture of a diffuse lumbar arachnoiditis. Laminectomy was performed and the arachnoiditis confirmed; the roots of the cauda equina were separated and the dura was left open after a section of tantalum foil had been placed over the roots.

Operation relieved the sensory changes, but sphincteric function did not return and lumbosacral pain persisted, as did motor impairment of the lower limbs.

Postoperative x-ray examination revealed an osteomyelitis of the first sacral to the second lumbar vertebral bodies, inclusive. No causative organisms could be identified.

From a review of the literature, the authors conclude that the rate of infection in the production of complications following caudal anesthesia is second only to the introduction of the analgesic agent into the subarachnoid space. HENRY A. SHENKIN, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Smithy, H. G.: Mixed Malignancy of the Breast. *Surgery*, 1944, 16: 854.

The simultaneous occurrence of two different malignant processes at points of origin quite distinct and separate from each other is a well established entity. Much less common than these anatomically unrelated tumors is the presence of two different types of neoplastic tissue growing within the same organ.

Mixed malignancy of the breast can be divided into two categories: (1) the simultaneous presence of two distinct varieties of malignant tumors growing side by side but having no structural intermingling of their elements, and (2) a combination growth of two different malignant tissues, the component parts of which are intimately blended with one another into a single tumor. The first type may be regarded as a coincidental occurrence of two independent neoplasms in the same organ, but the second type of mixed tumor of the breast can hardly be considered as an accidental coexistence of different neoplastic lesions. It appears likely that these tumors either arise from a single cell, or one element occurs first and subsequently stimulates proliferation of the other.

Experimental observations lend support to the possibility that a malignant lesion of epiblastic origin can stimulate adjacent mesoblastic elements to proliferate, and vice versa. Widely divergent opinions prevail among pathologists concerning the possibility that combination growths can originate from a single cell, and no positive expression can be made at this time.

The authors report in detail an unusual case of mixed sarcoma and adenocarcinoma in a ten-year-old negro girl. The case is believed to be the first of its kind recorded in a child.

Regarding classification of the tumor, it is desirable to avoid such terms as carcinosarcomatodes, carcinosarcoma, and sarcocarcinoma, which have been employed to indicate the relative time of appearance of the different malignant components of a dual tumor, as well as the preponderance of one element over the other. Actually, the neoplasm described consisted of two well defined individual malignant tissues. Therefore, for the purpose of clarity, the authors suggest that it be called a mixed sarcoma and adenocarcinoma. The word "mixed" is an important qualifying descriptive factor designed to differentiate the tumor from a condition in which the sarcomatous and carcinomatous growths exist as separate, independent neoplasms in the same breast.

The development of a dual mammary neoplasm in a patient at ten years of age is extraordinary. Only 4 authentic cases of carcinoma of the breast have been reported as occurring before puberty.

While removal of the breast was considered necessary, it was the impression of several examiners who saw the patient before operation that the lesion was benign, most probably mammary hyperplasia of an extreme degree. Accordingly, a simple mastectomy was done. In general, mammary sarcomas rarely invade the axillary lymph nodes so that axillary dissection is generally considered illogical in the operative treatment of this lesion, removal of the breast and pectoral muscles being the procedure of choice. Discovery of the carcinomatous factor was made only after sections of the axillary lymphoid tissue were examined. The involved lymph node was excised only because of its proximity to the incision, no attempt being made to dissect the axillary contents. Such being the case, the question arose as to the advisability of a second operation for removal of the pectoral muscles and the lymphoid structures of the axilla and the supraclavicular space, after discovery of the metastatic carcinoma. Probably such a radical procedure should have been carried out, but factors beyond control prevented it.

JOSEPH K. NARAT, M.D.

TRACHEA, LUNGS, AND PLEURA

Bird-Acosta, I.: Pulmonary Suppuration Secondary to Cardiospasm. *Am. J. Roentg.*, 1944, 52: 481.

Pulmonary suppuration as a result of esophageal overflow has often been reported in the literature. Esophageal retention may be caused by carcinoma of the esophagus, strictures, foreign bodies, pulsion diverticulum, extrinsic esophageal pressure from adjacent tumors, and cardiospasm. Of all the causes of pulmonary suppuration following esophageal overflow, cardiospasm, although a fairly common clinical entity, is rarely considered.

The author reports 3 cases of pulmonary suppuration as a result of cardiospasm.

MAURICE D. SACHS, M.D.

Davidson, L. R.: Hydatid Cysts of the Lung. *J. Thorac. Surg.*, 1944, 13: 471.

Hydatid cysts of the lung, while uncommon in this country (36 cases reported in the United States up to 1930), will, unfortunately, be much more frequent in the returning soldiers. The geographical distribution of this condition "is dependent on its incidence and distribution in reservoir hosts, particularly sheep, cattle, and pigs, and cases are most frequently seen in sheep-raising countries such as Argentina, Uruguay, New Zealand, Australia, Italy, Syria, Greece, and Algiers."

The life cycle of the echinococcus begins in the infected intestine of the definitive host (dog, wolf, or jackal) where the taenia are found. The untainted dog is infected by eating the organs of animals (intermediate or reservoir hosts, i.e., sheep or pigs) infected

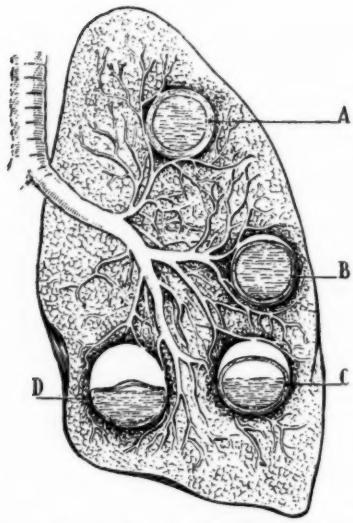


Fig. 1. A, Hydatid cyst of lung; B, perivesicular pneuma; C, double-dome arch (Cumbo's sign), and D, camalote formation (From José Arce).

with fertile hydatid cysts. Man, while also an intermediate host, represents a dead end as far as the further development of the parasite is concerned as his flesh is never eaten.

The taenia echinococcus which resides by the thousands in the intestine of an infected dog is a four-segment tapeworm about 0.5 cm. long. From the terminal proglottid, innumerable ova are discharged which gain entrance into man through contaminated water or vegetables. The egg lodges in the human stomach where the embryo is freed when the coat is digested by the stomach acid. It then migrates through the gastric or duodenal wall, enters the venules, and is carried to the first barrier—the liver. There the embryo enters the larvated stage and, in growing, empties its center and forms a fluid-filled vesicle with an inner or germinal layer and an outer or laminated layer. From the former layer vacuolated masses of cells (brood capsules) protrude into the vesicle's cavity. These in turn give rise to scolices. Most of the capsules and scolices are pinched off the germinal layer and sink in the hydatic fluid to form "hydatid sand." As the vesicle grows it stimulates in the organ the formation of an adventitial layer of connective tissue which is separate from the vesicle but is part of the simple hydatid cyst. If the cyst were in a sheep and the infested organ were eaten by a dog, the ingested scolices would enter the small intestine to become new taenia.

Daughter cysts, usually sterile and without scolices or proliferating vesicles, are generally the result of mechanical, infectious or toxic influence. On the other hand, an infected cyst, if ruptured or aspirated, may discharge scolices into surrounding tissue and cause secondary cysts (secondary hydatidosis). Therefore, when operating one must not permit any hydatid fluid or sand to contaminate the incisional or operative wound. For the same reason, one should never aspirate a cyst except at time of operation. If a primary cyst erodes the pulmonary vein, metastatic hydatidosis results.

The simple cyst fluid and membranes are sterile. If they enter a new phase and become complicated, infection causes death of the cyst and the contents of the cyst are necrosed and fragmented, and the vesicle virtually falls apart.

In the lung the vesicle is surrounded by adventitia and also a concentric layer of atelectasis. If on enlarging the cyst breaks into a bronchiole the perivesicle space communicates with the bronchiole. With coughing and straining, air may surround the vesicle and give a perivesiculum pneuma (B). If a larger opening occurs, air may enter the vesicle and produce Cumba's sign (C), a double-domed arch. Finally, when the membranes sink into the cavity and float upon the remaining fluid, the camalote (D) formation is noted. These are considered pathognomonic roentgenographic findings for pulmonary hydatid cysts. (See Figure 1.)

For diagnosis one must recognize the difference between simple and complicated cysts, which may be either peripheral or central. The simple cyst is usually silent. Nonproductive cough is the first symptom. There usually is accompanying chest pain. Later there may be hemoptysis with a productive cough. When the cyst enlarges dyspnea may be manifest. Physical examination often suggests the diagnosis. In case of doubt the place where a patient lives is of utmost importance.

Laboratory methods are of some value in diagnosis but the procedures are not unequivocal. Eosinophilia is not present in dead or suppurating cysts. An eosinophilia (over 4 per cent) may not be present even in living cysts. The complement-fixation test (Weinberg) and the more reliable intradermal test of Casoni are not infallible. Certain diagnosis is made only when hooklets, scolices, or laminated membranes are found in the sputum. Characteristic x-ray findings may establish the diagnosis even in complicated cases. Cysts are usually in the lower lobe and occur more frequently in males.

Medical treatment is of no value in echinococcus cysts; surgery is the only satisfactory method of treatment. The presence or absence of pleural adhesions determines the type of surgical treatment, the essence of which is opening the chest, incising the cyst, and removing the membranes. The one-stage operation in the absence of adhesions is neither simple nor without definite risk, particularly that of pneumothorax. Central cysts are only attacked when they are draining poorly or when accompanied by fever, and then only with caution.

The chest wall is opened over the cyst and the presence or absence of adhesions determined. These

may be shown preoperatively by a pneumothorax, but one may rupture peripheral cysts by pneumothorax. The cyst is entered and the membranes and contents are removed. Adhesions may be formed by packing the wound with gauze and reoperating two weeks later. A one-stage operation for an unadherent lung is accomplished by projecting the lung through the wound in the perietal pleura by using a tight-fitting mask and increasing the positive pressure to 10 cm. of water at the appropriate time. The lung, if unadherent, may be sutured to the pleura outside of the cyst area to prevent pneumothorax.

The cyst may be treated in several ways. The wounds are draped meticulously before the cyst is opened. Fluid is withdrawn with an aspirating needle and 2 per cent formalin is injected. The cyst wall is incised and the membranes are extracted from within the adventitia. The adventitia then may be completely sutured in a simple aseptic cyst, but in most cysts marsupialization to establish drainage is the procedure of choice. Fluid is not always obtained in a complicated cyst.

It is not unusual to have a simple cyst leak and rupture into a bronchus or bronchiole. If this progresses, the fluid and the membranes may be extruded and permit a spontaneous cure. If only the fluid is expelled the membranes remain and one may expect an infection or abscess formation.

The author then reports 4 cases. In the first a simple cyst was removed surgically with complete recovery. In the second case there was an intrathoracic hydatid cyst which may have arisen in the pedicle, body, or lamina of the vertebra. The chief complaints were due to cord compression. The patient was operated on twice and is now working as a laborer, without a brace. In the third case there was a complicated hydatid cyst of the left upper lobe; this was completely cured by operative drainage. In the last case there was a central hydatid with pneumothorax. Surgical drainage of the chest cavity only was attempted because of the central location. The patient died of a generalized peritonitis six months later without autopsy. ROBERT BIGELOW, M.D.

Rienhoff, W. F., Jr.: Present Status of the Surgical Treatment of Primary Carcinoma of the Lung. *J. Am. M. Ass.*, 1944, 126: 1123.

Reinhoff reports a clinical analysis of, and the results in, 181 consecutive cases of primary carcinoma of the lung in which operation was performed over an eleven-year period. Of this group 71, or 39 per cent, were operable. The sex incidence was 6 to 1 in favor of males; the incidence of involvement of right and left sides was approximately the same. Sixty-four of the patients were in the fourth to sixth decades, inclusive. The signs and symptoms that predominated in the order of their frequency were cough, hemoptysis, pain, weight loss, hyperpnea, pneumonitis, and fever. In general, there are no characteristic signs and symptoms of this disease—the lesion masquerades as many of the commoner disorders of the lung.

In this series of 181 cases the roentgenogram of the chest was positive in every instance. This diagnostic measure is the most important and the simplest method of examination. Second to x-ray study is bronchoscopy.

In 70 per cent of the cases subjected to pneumonectomy there were metastases to the bronchial and tracheal nodes.

The microscopic appearance of these lung tumors made it possible to divide them into two large groups: (1) the flat and (2) the squamous-cell carcinomas. The former gave a better prognosis.

The surgical treatment consists of total pneumonectomy. In this series 95 total pneumonectomies were performed, the immediate mortality being 25 per cent. Thirty-five per cent of the patients surviving are alive and well from one month to eleven years after the operation.

An otherwise fatal disease, primary carcinoma of the lung can be satisfactorily treated by surgical removal of the entire organ. Surgical measures short of total pneumonectomy are not efficacious. Postoperative mortality and longevity are at least as good as, if not better than, the postoperative results following the surgical treatment of carcinoma of other organs. J. M. MORA, M.D.

Kent, E. M., and Sager, W. W.: Current Practice in the Treatment of Thoracic Empyema. *Surg. Clin. N. America*, 1944, 24: 1492.

The authors described their management of thoracic empyema at the United States Naval Hospital, Bethesda, Maryland. The choice between open and closed drainage is discussed. Open drainage is preferred when localization has occurred and when the pus is thick, such as in pneumococcal infections. When the pus is thinner, especially with organisms such as the streptococcus or staphylococcus, and when the empyema space is a large one they prefer closed drainage. By closed drainage is meant the insertion of an intercostal tube or catheter, the distal end of which is placed under water. Later on it may be necessary to resect a rib and drain the cavity by open drainage. Tidal drainage may be used especially with the closed type of drainage when pus and fibrin obstruct the catheter.

It is estimated that 80 per cent of pneumonias are caused by the pneumococcus and the remainder by a variety of organisms. This holds true for empyema also, but there is some variation from year to year and from place to place. Before the use of sulfonamides in the treatment of pneumonia, the incidence of complicating empyema was from 5 to 6 per cent, but since the use of the sulfa drugs the incidence of complicating empyema is from 1 to 2 per cent. This decrease in the occurrence of empyema is found chiefly in the pneumococcal infections.

The fundamental principles are the same in both types of drainage. It must be carried out in a dependent position and maintained by close management. The tube must not become obstructed by fibrin or granulations; it should be shortened as the

cavity becomes obliterated rather than by a routine method for all cases. If the tube should slip out it must be replaced soon, because the opening in the chest wall contracts within a few hours and it may be impossible to reinsert another. The size of the cavity may be determined by filling it with sterile solution at intervals, or by x-ray examinations. The tube should be left in place until the space holds less than 10 cc.

When an empyema has formed under sulfa treatment for the primary lung infection it is often atypical. It may be loculated, nondependent, or interlobar, and often requires more than one drainage. However, the use of the drug decreases the incidence of empyema, and if thin fluid forms it may be sterilized without the formation of thick pus. The local use of the sulfa drugs is of questionable value.

Next to the pneumonias as the primary cause of the pleural infection is the intra-abdominal suppuration with subdiaphragmatic abscess and, later on, supradiaphragmatic extension. The organism here is often the colon bacillus.

The treatment of empyema with penicillin is not yet entirely standardized but the experience to date is sufficient to lead to certain conclusions which, however, may need to be revised at a later date. The best chances of success are in the early thin effusions before frank pus is formed. Of course, the type of organism and its vulnerability to penicillin are the main factors which will determine its successful use. Both parenteral and local use should be resorted to as parenteral use alone does not give high enough concentrations in the pleural cavity. Five hundred units per cubic centimeter is the concentration for local instillation. The pus should first be aspirated and one-half that volume of penicillin used for replacement.

Once frank pus is formed, drainage is usually required as thick pus and fibrin masses cannot be aspirated. Even though the cavity may be sterilized there remains the thickened pleura and fibrosis which lead to chronic empyema. Cases of penicillin failures are illustrated.

The development of bronchopleural fistula as a complication of empyema is a serious one and may lead to months of convalescence. When the x-ray film demonstrates a fluid level and when air has not been allowed to enter the pleural cavity a fistula must be assumed to be present. Early recognition is important, as closed drainage will often cause a spontaneous closure of the fistula. In cases in which the fistula does not close the morbidity is high and chronic empyema usually results. For such cases Blades is quoted as using a decortication operation through an intercostal incision, and the incision is closed tightly with closed catheter drainage and suction. The released lung may be readily expanded and caused to adhere to the parietal pleura. Should the fistula reopen it is of relative unimportance as the lung has adhered to the thoracic wall.

FORREST D. DODRILL, M.D.

HEART AND PERICARDIUM

Elkin, D. C.: Wounds of the Heart. *Ann. Surg.*, 1944, 120: 817.

This report concerns the operative treatment of 23 cases of wounds of the heart, or intrapericardial portions of the great vessels. There were 5 deaths in this series, a mortality of 22 per cent, as compared with a 42 per cent mortality in a previously reported series of 38 similar cases. In the present series there were no deaths from infection. Those patients who did not recover either died on the operating table, or shortly after operation, presumably from hemorrhage or the effects of tamponade. The reduction in mortality from infection was not due to the use of sulfa drugs, since they were used in only 1 case for the treatment of postoperative pneumonia. In no instance was a sulfa drug placed in the wound. The reduction in infections is believed to be the result of more careful preoperative preparation and a more meticulous technique. Another possible factor in the lowered mortality has been the giving of intravenous fluids to the last 8 patients prior to operation. This treatment was based on experimental evidence that rapid intravenous infusion, with subsequent increase in the blood volume, enables a dog to withstand a considerably higher intrapericardial pressure. In each patient receiving intravenous infusions there was clinical improvement preoperatively.

The indication for operation in all cases was the finding of definite evidence of cardiac tamponade. This diagnosis was based on lowered arterial and increased venous pressure, and the presence of a quiet heart on fluoroscopic examination. The latter finding is the most important sign and the one least likely to lead to a mistaken diagnosis. Venous-pressure readings are not only of value in the diagnosis of tamponade but are of considerable prognostic importance. If the venous pressure is high, that, in itself, is evidence that the heart is carrying on its functions and that the cardiac output is at least sufficient to produce such pressure. On the other hand, a low or lowered venous pressure in the presence of tamponade is evidence of a failing heart and a greatly reduced cardiac output. In 17 patients arterial pressure was so low that it could not be recorded. In those patients who recovered there was an immediate rise in arterial pressure following the release of the tamponade. Some type of general anesthesia in which positive pressure can be used is preferable to local anesthesia, since the difficulties of heart suture require that the patient be quiet throughout the procedure.

The author has slightly modified his previous opinion that operation should always be performed as soon as the diagnosis of a heart wound is established. Delay is justified if continued improvement follows aspiration without recurrence of signs of cardiac compression, but operation should not be delayed if there is evidence of bleeding into the pleural cavity or through the external opening. In this series, all patients had immediate operation. A

tabulated summary of the data on the 23 cases is presented. JOHN L. LINDQUIST, M.D.

Yódice, A.: The Surgical Treatment of Cardiac Syncope, Apparent Death, Cardiac Fibrillation, Stoppage of the Heart (Tratamiento quirúrgico del sincope cardiaco. Muerte aparente, fibrilacion cardiaca, paro cardiaco). *Rev. As. méd. argent.*, 1944, 58: 931.

During operation with any kind of anesthesia, cardiac syncope may occur. The heart beat stops and there is no arterial circulation. This condition may result from ventricular fibrillation or stoppage of the ventricle. The pressure falls to zero. The patient is apparently dead, although prompt action may restore the heart beat. The brain cannot endure deprivation of the blood supply for more than from two to five minutes and therefore action must be very prompt. Every second counts. Efforts are being made to find some means of preserving cerebral function for a longer time but so far they have not been successful. Experiments in producing artificial fibrillation in animals and then treating it have contributed to the successful treatment of this condition in human beings.

In every operating room the apparatus for treating stoppage of the heart should be at hand. If the heart stops the anesthetist should give artificial respiration to keep up the oxygenation of the lungs, while the surgeon should expose the heart by opening the pericardium and massage the heart with a rhythm of from 50 to 60 movements per minute. After the flabbiness of the heart muscle has been overcome and the beat restored, electrical shock should be given for the purpose of overcoming the fibrillation. The apparatus used for this purpose is illustrated and the technique of the shock described in detail. The shock may be applied 3 or 4 times, or even more if necessary. Patients apparently dead have been restored in this way. Illustrative cases are described.

Supplementary methods are the pouring of 2 cc. of a 5 per cent solution of procaine over the heart before the massage and the injection into the cavity of the right ventricle of 1 cc. of a 1:1000 solution of adrenalin diluted in from 10 to 20 cc. of physiologic salt solution, if massage does not prove effective at first. AUDREY G. MORGAN, M.D.

ESOPHAGUS AND MEDIASTINUM

Rankin, L. M. Perforated Ulcer of Esophagus Following a Burn. *Am. J. Surg.*, 1945, 67: 134.

In 1842, Curling first described duodenal ulcer following a burn. The cause and frequency of this complication are still uncertain. Ulceration of the lower end of the esophagus following a burn is even more rare. A search of the literature revealed only 1 case of perforation of such an esophageal ulcer.

The author presents the case of a four-year-old boy who sustained second-degree burns of both thighs, buttocks, and the lower abdomen. The child progressed very well for four days. He then suddenly developed severe pain, following which his condition became worse, and he died within two hours. Autopsy revealed a perforated ulcer of the lower end of the esophagus with hemorrhage (Fig. 1).

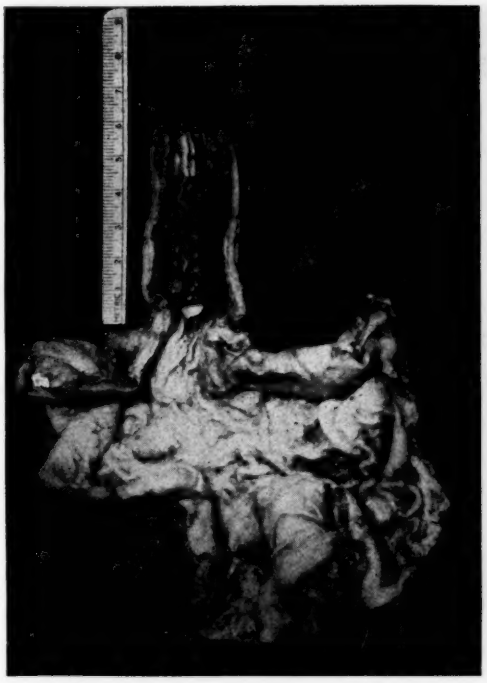
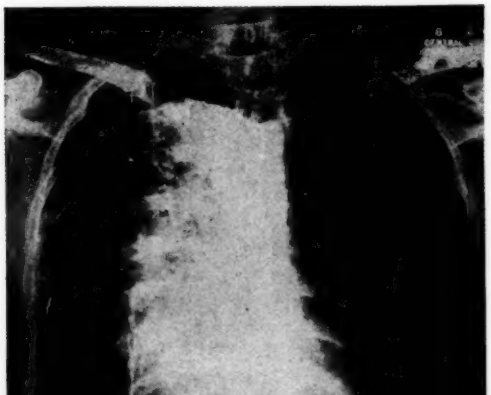


Fig. 1. The lower end of esophagus and stomach showing perforation of ulcer of esophagus. (Courtesy of American Journal of Surgery.)

No case has been reported in which surgical closure has been attempted, but this gives the only hope for cure. THOMAS F. THORNTON, JR., M.D.

Hurst, A., and Bassin, S.: Megaesophagus as a Cause of Mediastinal Widening. *Am. J. Roentg.*, 1944, 52: 598.

This report deals with 11 cases in which the initial roentgenogram of the chest suggested the presence of a megaesophagus, which was subsequently verified by a barium meal. They were discovered in extensive mass surveys of apparently healthy adults to detect unknown cases of tuberculosis. Nine patients were males, inasmuch as the majority were rejected draftees. One of the most interesting features in the study of megaesophagus is the marked disproportion between the relative paucity of the complaints and the good general condition of the patient on the one hand, and the large size of the esophagus on the other. No benign or malignant



stricture causes dilatation even approaching that produced by "cardiospasm."

Five diagnostic roentgen features were found, as follows:

1. Diffuse widening of the mediastinum. The shape depends largely on the degree and location of the dilatation. The widening of the mediastinum is usually seen beginning at the thoracic inlet or just below. The degree of widening is difficult to measure since the largest dilatation is to the right and the left border is lost in the density of the heart shadow.

2. A definite fluid level was found in 4 of the 11 cases traversing the tracheal column of air at the level of the clavicles. This depends for its presence on recent drinking or eating, but if present is pathognomonic.

3. In the upper esophagus lying to the right of the sternum, there is occasionally seen a peculiar stippled, marbled or mottled density. This is due to the contrast created by the mixture of air and food contents. It was seen in 4 of 11 patients.

4. All but one case showed apparent widening of the cardiac contour on the right. Greater exposure reveals an apparent reduplication of the cardiac contour.

5. In all cases the dilated esophagus, after following the cardiac contour, crossed to the left and obliterated the cardiophrenic angle.

In suspected cases complete roentgen studies with barium should be made to differentiate this condition from congenital anomalies involving the esophagus and stomach.

THOMAS F. THORNTON, JR., M.D.

SURGERY OF THE ABDOMEN

GASTROINTESTINAL TRACT

Milanes, F., Vega, T., Morales, E., Rodriguez, A., and Diaz, A. R.: Total Gastrectomy; a Clinical and Physiopathological Study. *Gastroenterology*, 1944, 3: 380.

Thirteen total gastrectomies were done by the authors during the period from 1941 to 1944 inclusive. The effects of total gastrectomy are briefly stated following studies on 4 of their patients who survived long enough to be in a good general condition. Comments are made only on results as a whole and the details are omitted. The immediate postoperative mortality was 27 per cent. The total mortality in cases of malignancy was 91 per cent within a period of one and a half years after operation. The average duration of life was ten months. One patient is still living after three years.

The authors consider total gastrectomy for malignancy only in well selected cases. The most favorable lesion is the linitis-plastica type of carcinoma, without metastasis, in a middle-aged patient in good general condition. High lesser-curvature ulcers are also suitable for total gastrectomy. Absence of metastatic involvement is necessary. The resection must be total, with the cardia and pylorus visible in the specimen.

The authors are now more pessimistic than they were when they began this type of treatment and believe that the average survival period is not longer than one year, which does not sufficiently reward the patient for his effort. In their experience, in general, it is advisable to perform subtotal partial gastrectomy for the surgical treatment of cancer.

The physiopathological results in total gastrectomy are shown in table 1 in a review of their 4 cases. The chief disturbance which follows total gastrectomy is motor in character. The general metabolism may be preserved and the mineral metabolism is only slightly affected. Anemia may occur, especially the hypochromic type. Attention must be given to the diet and pharmacal measures to protect the nutrition.

EMIL C. ROBITSHEK, M.D.

Feasby, W. R.: Peptic Ulcer in the Canadian Army (1940 to 1944). *War Med.*, Chic., 1944, 6: 300.

In this report on the dyspeptic syndromes in the Canadian Army, gastroduodenal disorders accounted for only 1 per cent of the total admissions to the hospital but they utilized one-eighth of the beds in the medical inpatient division. Only patients with respiratory-tract disease were more numerous among hospital admissions.

An accurate diagnosis among recruits was difficult because only fifteen minutes were available for clinical examination. Even with this limited time the per cent of error was only 12 as revised by x-ray study. The length of the history was not always helpful because some patients had very short histories—one being only five days. Psychoneurotics, morons, and malingerers made an accurate diagnosis difficult, malingerers being the most troublesome.

At first an attempt was made to return men with healed duodenal ulcers to active duty, but only 8 of 70 such patients could remain on duty in England. Then an attempt was made "to determine how healed peptic ulcer patients would be able to carry on with some duty in Canada." This study showed that some 10 per cent of these men could remain on active duty. Two factors were important in their ability to do this: (1) willingness to continue in service, and (2) the ability to select food and environment. It was interesting to note that officers and noncommissioned officers made up half of this group.

Gastric ulcers made up 7 per cent of the total, and all of the patients with healed gastric ulcer were unable to continue on duty in England which necessitated ultimate discharge from the service.

From this study the author has concluded that the incidence and significance of peptic ulcer in the army have been overestimated, and that the cause for this is the failure to recognize that military hospitals classify their patients into medical and surgical groups. In addition, large outpatient clinics are also conducted. Both parasitic and traumatic illnesses exceed gastrointestinal disease in importance. The author recommends that patients having perforation or hemorrhage be excluded in order to reduce pension responsibility. Moreover, the treatment of peptic ulcer should be undertaken in special units. Segregation of these patients provided a most economical and satisfactory method for their care. The author's final conclusion was as follows: "The usefulness of persons suffering from peptic ulceration, whether they are with the armed forces or in civil occupations, is limited. They have a disease which causes serious wastage of man hours and enough misery to warrant the best study possible."

SAMUEL J. FOGELSON, M.D.

Hunt, G. H., and Bowden, J. N.: Rupture of Intestine Caused by Nonpenetrating Trauma of the Abdominal Wall: A Report of Cases. *Arch. Surg.*, 1944, 49: 321.

This report of 6 cases of rupture of the intestine caused by nonpenetrating trauma of the abdominal wall is principally concerned with the results of relatively minor trauma. With the type of injury considered there is likely to be an interval of several hours during which abdominal symptoms are minimal and signs confusing. The symptoms are those of peritonitis, which develop with variable rapidity, according to the site of perforation, the composition of the leaking intestinal contents, and the amount of leakage. Shock is generally not an outstanding fea-

ture in these cases, but some pain is usually present from the beginning. The two important points are: (1) keeping the possibility of intestinal perforation in mind following even minor trauma, and (2) prompt exploration of the abdomen at the first sign of peritonitis. The operative procedure is planned to permit thorough exploration of the entire small intestine, since most perforations occur in the jejunum or ileum. If a perforation is found, it should be covered with a warm, moist sponge, and possible multiple perforations sought.

Six cases are reported in detail. In one of these the intestinal perforation was complicated by other serious injuries which masked the abdominal symptoms and precluded exploratory operation after abdominal symptoms did appear. Another case was accompanied or caused by penetrating trauma. In 4 cases of uncomplicated rupture of the intestine by nonpenetrating abdominal trauma, the mortality rate was 25 per cent; in all 6 cases the mortality rate was 33.3 per cent. JOHN L. LINDQUIST, M.D.

Spelman, A. E.: Healing of Intestinal Anastomosis. *Am. J. Surg.*, 1944, 66: 309.

The author reports the results of his studies and describes the essentials of the process which establishes continuity of the gastrointestinal tract following either the suture of wounds or an anastomosis. The more common factors causing failure are also presented. The material consisted of pyloric resections, gastroenterostomies, and intestinal anastomoses performed on more than 100 dogs. Serosa-to-serosa approximation by suture was performed on more than 50 rabbits. Varying techniques were used in suturing; some specimens received meticulous aseptic care, others being contaminated with bowel contents. This investigation was further limited to the following procedures: (1) those accomplished without contamination by virulent organisms; (2) those in which unattenuated organisms may produce infected areas; and (3) those attempted in the presence of a deficient blood supply.

Healing was studied after the intestines were sutured with one continuous silk or chromic catgut inverting stitch, including the mucosa, muscularis, and serosa. Another silk stitch included the serosa only.

When the gut wall is inverted by suturing, a triangular chink is formed just outside of the line of anastomosis on the serosal side. Within fifteen minutes fibrillar fibrin begins to form in the exudate, which binds the surfaces together and makes them watertight.

During the first few days following the anastomosis there is hyperemia, general edema, and cellular infiltration in the tissues of the sutured area. This leads to tissue which pushes the serosal surfaces into closer approximation, and thus aids in the closing of the chink along the line of anastomosis. The general swelling enlarges the volume of tissue and by its size may produce a brawny thickening of the ring, which causes partial occlusion of the lumen. After a week the swelling begins to subside and in another ten days it has largely disappeared.

Infection with virulent organisms causes granular fibrin to form. The wound may be temporarily sealed by the granular fibrin; but before permanent union of the tissues takes place, it undergoes resolution and the tissue surfaces are freed. The wound then may be easily pulled apart, and may leak if the suturing and consistency of the tissue is not sufficient. This dissolution of union occurs most often between the sixth and eighth days.

When the circulation to the stomach was impaired and a posterior Polya type of anastomosis was made in dogs, they recovered from the operation and improved rapidly until, by the fifth day, their condition appeared almost normal; then invariably the animals died rather suddenly between the sixth and eighth days.

A study of specimens of this type showed that within twenty-four hours the exudate and fibrillar formation were present, but the latter soon underwent resolution as necrosis developed in the ischemic area.

This study, therefore, demonstrates that the most tangible aids in establishing a watertight anastomosis were fibrillar fibrin, lack of contamination with virulent organisms, and an adequate blood supply to the area of anastomosis. Every effort should be made to avoid localized areas of ischemia, particularly when the blood supply has already been decreased. SAMUEL J. FOGELSON, M.D.

Anderson, S. G.: A Statistical Survey of Appendicitis in Children. *Med. J. Australia*, 1944, 2: 567.

An analysis is presented of 933 cases of acute appendicitis treated at the Children's Hospital, Melbourne, between 1931 and 1943. Fifty-five patients were under the age of three years (younger age group), and 878 patients were between the ages of three and fourteen years (older age group).

Complications of abscess or peritonitis were present in 75 per cent of the 55 patients under the age of three years, and in 30 per cent of the 91 patients between the ages of three and six years.

In the younger age group 68 per cent of the patients had temperatures over 102°F., and in the older age group 13 per cent registered fever of this degree. Twelve patients in the older age group with appendical abscess or general peritonitis, and 103 patients with acute appendicitis had normal temperatures on admission.

Vomiting preceded abdominal pain in the majority of the patients in the younger age group, whereas abdominal pain was the first symptom in the older age group.

Sixty-five per cent of the patients in the older age group were hospitalized for less than ten days, and 32 per cent were in the hospital for more than ten days. Infection of the wounds was the cause of prolonged convalescence in 83 per cent of the cases.

Infection of wounds was studied in 185 consecutive patients in whom this complication occurred,

and in the majority of these (153) there was some degree of peritonitis at the time of operation. Nonpurulent fluid was present in the peritoneal cavity in 17 patients, and intraperitoneal drainage resulted in infection of the wounds. This was in contrast to many similar cases in which the abdomen was closed without drainage and without subsequent infection of the wound. In the cases in which there was some degree of purulent peritonitis at operation, the smallest percentage of infections of the wounds was noted among the patients in whom the abdomen was closed without drainage—17 per cent of wounds were not infected after intraperitoneal drainage compared to 48 per cent after no drainage.

The mortality figures were as follows:

Type of Condition	No.	Deaths
Children under three years of age		
Acute appendicitis	14	0 (0%)
Acute appendicitis with abscess or peritonitis	41	16 (39%)
Children over three years of age	878	24 (3%)

Twenty-two of these deaths occurred in cases complicated by peritonitis or appendical abscess.

In the younger age group a study was made of the mortality in cases complicated by peritonitis or abscess. Of the 11 patients with peritonitis, 4 died (36 per cent). There were 18 abscesses, and in one-half of the patients the operative technique involved disturbance of the localizing barriers, with 6 deaths (67 per cent); in the remaining half the operative disturbance was minimal (2 appendixes not removed) and there were no deaths; the operative findings were inconclusive in the remaining 12 cases.

The influence of sulfonamide drugs as an adjunct in treatment was inconclusive because of the small number of cases in which they were employed.

ERNEST E. ARNHEIM, M.D.

Moreno, I. G.: Transperitoneal Fixation of the Kidney and Colon (Nefrocolonfijacion transperitoneal). *Bol. Acad. argent. cir.*, 1944, 28: 1063.

The author, in collaboration with Russo, has operated by the transperitoneal route for fixation of the prolapsed kidney and colon. The patients were between twenty-five and thirty years of age and mostly women. Nine of them returned for examination, and a number of pyelograms made before and after operation are shown. The case histories are given. In 90 per cent of the cases all symptoms disappeared. No patient was made worse by the operation. In 50 per cent of the cases there was no constipation before operation, and 90 per cent of the existing constipation in the remaining cases was corrected. Increase in weight after the operation varied from 5 to 13 kgm. Elevation of the kidney was not brought about in 2 cases, but the patients were cured of their symptoms. There was a moderate lifting of the colon in all the cases.

The operations were performed by the technique of Alberto Gutiérrez. It was found, however, that when the quadratus lumborum and psoas muscles were sutured vertically the muscles tore easily; therefore, they were sutured transversely and to include a large amount of muscle in the suture. Otherwise the kidney overcomes the suture and becomes displaced again. The appendix can be removed at the same time, as it sometimes plays a part in causing the patient's symptoms. The author believes that more can be accomplished by the transperitoneal route in this condition than can possibly be accomplished by the lumbar route, and that this operation is infinitely superior to any of the other operations proposed for prolapse of the kidney and colon.

AUDREY G. MORGAN, M.D.

Mackenzie, D. H.: Sulfasuxidine in Operations on the Rectum and Colon. *Brit. M. J.*, 1944, 2: 722.

Various workers have shown that the administration of succinyl sulfathiazole (sulfasuxidine) causes profound changes in the stools of the recipient, the principal change being a marked decrease in the gram-negative organisms of the intestine, as shown by colony counts and by the study of films.

In connection with the surgery of the rectum and colon, some investigations have been made to determine the action upon the intestinal organisms of sulfasuxidine, sulfaguanidine, and sulfathiazole. The technique used was that of Holt and Wright, namely, 0.5 gm. of feces was thoroughly mixed with 4.5 cc. of nutrient broth and serial dilutions were made up to 10^6. One standard loopful of each dilution was plated on to selective media—MacConkey and desoxycholate citrate agar. Colony counts were made after twenty-four hours at 37°C. Films were examined wet and with Gram's stain.

The author investigated 30 cases. These were studied as follows:

3 cases	received	20 gm.	per day	of sulfasuxidine
5 "	"	10 gm.	"	"
8 "	"	10 gm.	"	sulfaguanidine
6 "	"	2.5 gm.	"	sulfathiazole
8 "	"	5 gm.	"	"

An account of the results is given. They were remarkably consistent. In the cases receiving 20 gm. per day of sulfasuxidine, colony counts and studies of films showed a universal decrease in gram-negative organisms. In cases receiving 10 gm. per day the "sterilization" was less consistent and more time was required to effect an adequate reduction in gram-negative organisms. The dosage of 5 gm. per day appeared to be ineffective.

The action of sulfaguanidine in no way compared with that of sulfasuxidine, with the exception of the abolition of pathogenic nonlactose fermenters. Even after five or six days' treatment there was frequently a confluent growth of coliform organisms when the 10^1, 10^2, and sometimes the 10^3 dilutions were plated out.

The use of sulfathiazole as a preoperative treatment has certain obvious disadvantages. It is more likely to cause toxic symptoms than either sulfasuxidine or sulfaguanidine, and is far more likely to give rise to renal complications. However, even with the

small doses given in these experiments, there was a greater effect than that obtained with sulfaguanidine. There was a decline in gram-negative organisms, and with a dose of 5 gm. per day it was common for bacillus-coli colonies from the 10^2 dilution to number less than 20.

From these studies the author concludes that a dosage of 20 gm. of sulfasuxidine per day for four days before operation as a preoperative treatment, is satisfactory. MATHIAS J. SEIFERT, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Timoney, F. X.: Cholecystitis. The Advantages of Operative Treatment in Definite Unmistakable Disease. *Am. J. Surg.*, 1945, 67: 57.

Of the 151 patients with cholecystitis treated by the author, 90 were female and 61 were male. Seventy-six per cent of the patients were in the thirty-to-sixty-year age group. A reasonably high degree of diagnostic accuracy was obtained. The diagnosis was correct in all but 7 cases. This can be attributed to the presence of x-ray evidence of stone, repeated nonfilling of the gall bladder during cholecystography, or the history, with symptoms and definite physical signs of an acute attack.

Cholecystectomy was the operation of choice in more than 90 per cent of the cases. Six per cent of the patients required drainage of the common duct. The outstanding indications for common-duct drainage are palpation of stones, a history of jaundice, multiple small stones in the gall bladder with a dilated cystic duct, dilatation of the common duct, and enlargement of the head of the pancreas.

Operations performed in the presence of unmistakable gall-bladder disease give assurance of increased satisfactory results. This is the result of more strictly limiting the indications for operation. The presence of gall stones or the history or presence of an acute attack make reasonably certain indications for operation. The operative mortality for unmistakable gall-bladder disease can be kept to a low figure.

SAMUEL KAHN, M.D.

Mirizzi, P., and Urrutia, J. M.: Sequelae of Cholecystectomy (Secuelas de la colecistectomia). *Hospital*, Rio, 1944, 26: 501.

This is a study of cases in which symptoms recurred after cholecystectomy. It is based on the operations performed by the authors in the past ten years and 1,000 operations performed elsewhere. Graphs show the facts on which their conclusions are based.

They found that cholecystectomy gives complete cure in 95.8 per cent of the cases, and that there are serious sequelae in 1.6 per cent and milder sequelae in 2.6 per cent. Most of the serious sequelae are due to residual stones in the common duct that have been overlooked on operation. Those of lesser seriousness are most frequently caused by spastic disturbance of the sphincter of Oddi and pancreatitis. Infection is a secondary and not a primary cause of the postoperative symptoms. It aggravates rather than produces the difficulty. Residual hepatitis is not an important factor in causing postoperative symptoms. It generally improves automatically after the cholecystectomy. Adhesions may cause serious sequelae but there are not many cases in which they are the only cause of the disturbance.

Surgical treatment should be complete in the first operation. Repeated operations are always more difficult and dangerous than the first operation. The best means of preventing the overlooking of any stones is by the use of operative cholangiography, that is, the taking of roentgenograms of the bile tract during operation. These are much more reliable than roentgenograms taken before operation and make accurate diagnosis possible in 99.5 per cent of cases; thus they reduce unpleasant sequelae to a minimum. AUDREY G. MORGAN, M.D.

Schena, A. T.: Rupture of the Common Duct after Choledochostomy (Ruptura del coledoco postcoledocostomia). *Bol. Acad. argent. cir.*, 1944, 28: 1030.

Rupture of the scar in the common duct after drainage for infection is rare. Only 8 cases have been described previously in the world literature and the author adds a ninth, on which he operated. The patient was a woman of forty-eight who about a year previously had been operated on for biliary lithiasis; the gall bladder was removed and the common duct drained with a Kehr tube. On the recurrence of symptoms she was operated on by the author and a residual stone was removed from the common duct and drainage again established with a Kehr tube. The tube remained in for a total of thirteen and one-half months. Some six months after removal of the tube signs of peritonitis developed and operation showed that infected bile was flowing into the peritoneal cavity from a rupture of the operative opening in the common duct. The pus was encysted, partly because of the presence of adhesions from the former operation, and the patient recovered.

The factors that bring about rupture of a choledochostomy scar are increased pressure within the duct and infection, which softens the cicatricial granulations and makes them friable. There may also be digestion of the tissues from activation of the pancreatic reflex, but there was no history of pancreatitis in this case.

The question of how long a Kehr tube should be left in place after a choledochostomy is a disputed one. Carter in 1936 published a review of the opinions of North American physicians. Judd said that the tube should remain in place as long as there are any signs of infection and that it does no harm if it remains for months. Schena held that the time should be determined by postoperative cholangiography and the functional tests of Bengolea.

In the discussion Allende said that the probable cause of the rupture was excessive denudation of the common duct during the operation, which deprived the wall of its vessels and led to mortification. This

may occur when it is difficult to free the common duct from a dense inflammatory infiltration, and it is particularly apt to occur when a second operation has to be performed as in this case.

AUDREY G. MORGAN, M.D.

Martiarena, L. H.: Tumor of Vater's Ampulla; Duodenopancreatectomy in One Stage (Tumor de la ampolla de Vater; duodenopancreatectomia en un tiempo). *Bol. Acad. argent. chir.*, 1944, 28: 1042.

A safe technique for duodenopancreatectomy with ligation of Wirsung's duct was not devised until 1935. The author describes a case of tumor of Vater's ampulla in a man of forty-three who for eight years had had attacks of alimentary intoxication. Following a very severe one with intense itching, icterus, and acholia he came for treatment. There was a palpable swelling in the right hypochondrium.

Operation showed a lobulated tumor in the head of the pancreas, extending back of the mesenteric vessels and connected externally with the wall of the second part of the duodenum. Removal of the tumor, after ligation of the vessels, and duodenopancreatectomy with suture of the stump of the pancreas with chromicized catgut were done. The steps of the operation are illustrated. The patient's condition improved under the administration of hypertonic glucose solution, the transfusion of blood, and injections of vitamin K. As a substitute for the pancreatic secretion he was given takadiastase and peptopancrease. The pancreatic fistula continued to drain for twenty-seven days and was completely closed forty days after the operation. Histological examination showed adenocarcinoma grade III of Vater's ampulla, adenocarcinoma of the pancreas, and metastatic adenocarcinoma of a retropancreatic gland.

When tumors of Vater's ampulla grow into the lumen of the duodenum they can be removed transduodenally. Among the 126 operations of this kind, 103 were performed before 1935 with a mortality of 33 per cent, and 23 were done since that time with a mortality of 17 per cent. Twenty-two of the patients survived three years or more. When the tumor is of the ulcerous type it often invades the inner wall of the duodenum and the head of the pancreas and necessitates duodenopancreatectomy. This operation was formerly performed in two stages but is now performed in one stage when the condition of the patient permits.

The dangers are pancreatic biliary or duodenal fistula and the risks due to the loss of pancreatic juice. The pancreatic fistula often closes spontaneously, but if it does not do so in a few weeks the stump of the pancreas should be implanted into the intestinal tract, most frequently into the stomach. The biliary fistula shows little tendency to close spontaneously and the best treatment is to anastomose the common duct with the intestine. So far as has been observed, from 80 to 85 per cent of the fat ingested is absorbed in man after loss of the pancreas. Definite conclusions as to the effect of the loss of pancreatic juice cannot be drawn until a number of patients have survived the operation for five years or more.

AUDREY G. MORGAN, M.D.

Mirizzi, P. L.: Biliary Lithiasis and Pancreatic Disease. A Contribution on Operative Cholangiography (Litiasis biliar y pancreopatía. Aporte documental de la colangiografía operatoria). *Prensa méd. argent.*, 1944, 31: 2241.

There is a very close relationship between biliary lithiasis and disease of the pancreas. Among 1,278 cases of acute pancreatitis reported by Schmieden and Sebening there was disease of the biliary tract in 894, or 70 per cent. Statistics reported by other authors give about the same proportion. This relationship is brought about by dystonia of Oddi's sphincter which results in the reflux of bile into Wirsung's duct, or, conversely, of pancreatic secretion into the bile tract.

Biliary lithiasis is a prominent factor in the causation of acute and chronic pancreatitis, and, conversely, the reflux of pancreatic secretion into the bile tract is a factor in the etiology of such diseases of the bile tract as perforation of the gall bladder, exfoliative cholecystitis, and biliary peritonitis. It is not the presence of the pancreatic secretion in the bile tract itself that causes the trouble but the fact that it changes the reaction of the bile from acid to alkaline and thus makes it a good medium for activating trypsin to the point where it digests the tissues.

This flow of fluid from the one system to the other can be demonstrated by operative cholangiography, that is, the injection of lipiodol into the cystic duct or vestibule followed by the taking of roentgenograms. These demonstrate the reflux.

Cases of the various diseases of the bile tract and pancreas caused by this reflux are described and illustrated.

AUDREY G. MORGAN, M.D.

Young, H. B.: A Case of Accessory Pancreas in an Unusual Position Complicated by Acute Necrosis. *Glasgow M. J.*, 1944, 142: 156.

A thirty-six-year-old male was operated upon for a suspected perforated ulcer. For three weeks he had had midepigastric pain of a stabbing type passing through to the back. This was accompanied by nausea and vomiting. On the day of admission to the hospital he suddenly developed very severe generalized abdominal pain. The abdomen was held rigid.

At operation a firm mass was found in the gastrohepatic omentum along the lesser curvature of the stomach, but completely separate from this organ. The mass was the size of a walnut, irregular, firm but not stony hard, and unconnected with any other structures. The lesser omental bursa was explored and found to be normal; the pancreas was not unduly hard or irregular.

A biopsy of the tumor mass was proved to contain pancreatic tissue including islets of Langerhans. There were areas of necrosis. The final diagnosis was infection of an accessory pancreas.

EARL O. LATIMER, M.D.

Miller, J. M., and Wiper, T. B.: Physiological Observations on Patients with External Pancreatic Fistula. *Ann. Surg.*, 1944, 120: 852.

During the past ten years there have been only rare reports appearing in the medical literature of physiological observations made upon human subjects with external pancreatic fistula. The fundamental information concerning pancreatic function has been derived from the experimental laboratory animal, on which, with painstaking care, the fundamentals of pancreatic secretion have been investigated. Rarely has the clinician been given the opportunity to correlate the physiological observations made upon the human being with the results obtained from the experimental animal. The recent advances made in the operative attack upon lesions of the pancreas make it imperative that the surgeon be more conversant with the physiology of that organ, for interference with the normal flow of the external secretion will result in profound alterations in the total metabolism.

A rare opportunity was offered to make observations on the influence of such persistent fistulas upon these patients, particularly with reference to the many alterations induced. The observations included:

(1) the general nutritional state of the patient; (2) the total pancreatic flow in twenty-four hours; (3) the pattern of flow in a twenty-four-hour period (4) the plasma-electrolyte pattern; (5) the plasma protein; (6) the influence of water intake on the pancreatic flow; (7) the observations on volume flow alterations induced by the administration of various substances into the duodenum; (8) the effect of intravenous fluids upon the pancreatic secretion; and (9) observations on volume-flow alterations induced by the subcutaneous administrations of drugs.

They are reported in detail in a statistical study presented in this article.

Pancreatic flow is continuous throughout the twenty-four-hour period and is influenced, to great degree, by the state of hydration of the individual. One pancreas produced 1,770 cc. of fluid in a twenty-four-hour period. Attention was drawn to the marked alteration in water balance, plasma-protein level, and plasma electrolytes, with special emphasis upon plasma sodium in patients with severe external pancreatic fistula. It was emphasized in this presentation that the sodium loss in severe pancreatic fistula produces a clinical syndrome similar to that described by Addison, with the exception that adrenal disease is not present. This analogy has not been stressed previously. The administration of adequate amounts of sodium and water in the presence of sufficient plasma protein to hold them in the circulation alleviates the symptoms peculiar to this syndrome.

Diminution in pancreatic secretion through the fistula may be obtained by the administration of a number of drugs. However, ephedrine and sodium bicarbonate are the most practical of these because of the unpleasant or deleterious side-effects of the others. Pancreatic secretion is markedly stimulated by the intramuscular administration of histamine, and by the intravenous administration of physiological saline solution or 5 per cent glucose in physiological saline solution.

Detailed physiological observations upon pancreatic function were recorded. Certain of these observations contribute definite support to the theory that secretin secretion is a filtration process. These are:

1. Sodium ion is present in equal amounts in both blood plasma and pancreatic secretion.

2. The total of the concentrations of chloride and bicarbonate ions are the same in blood plasma and pancreatic secretion.

3. The same amount of ionizable calcium is present in blood plasma and pancreatic secretion.

4. Sulfanilamide is found in the same amount in blood plasma and pancreatic secretion.

Large amounts of ionizable calcium are normally returned to the gastrointestinal tract through pancreatic secretion. This phenomenon has not previously received the recognition it warrants.

The appearance of sulfanilamide in therapeutic concentration in pancreatic secretion suggests its use in acute inflammatory disease of the pancreas.

JOHN E. KIRKPATRICK, M.D.

Erb, W. H.: Radical Pancreatoduodenal Resection for Adenocarcinoma of the Head of the Pancreas. *Surg. Clin. N. America*, 1944, 24: 1370.

The development by Whipple, Brunschwig, and others of a surgical technique for the radical removal of carcinoma of the head of the pancreas necessitates an earlier diagnosis so that more and more cases may be found to be operable at laparotomy. With this in mind, the author charted laboratory data, histories symptoms, and physical signs to aid in the differential diagnosis of surgical and nonsurgical jaundice of the hepatocellular variety. The diagnosis of hemolytic jaundice is usually sufficiently clear, and it is not included in the tables. If a definite diagnosis cannot be made, then surgical exploration is indicated. If the lesion is not surgical, the harm to the patient can be kept at a minimum with adequate preoperative preparation and continuous spinal anesthesia.

A woman, aged fifty-two years, had been well until a year before admission, at which time she began to complain of vague indigestion and gas pains. There was no recent history of jaundice or of pruritus. The Graham-Cole test sixteen hours after oral administration of dye failed to show any evidence of a gall-bladder shadow. The patient's clinical history and the presence of a small extrinsic pressure defect on the duodenal cap aroused the suspicion of early malignancy of the pancreas or common duct. Examination at this time revealed a mild icterus and a palpable mass in the region of the gall bladder. The Van den Bergh test was immediately direct, the icterus index 30 units, and the quantitative serum bilirubin 1.4 mgm. per 100 cc. of serum.

Under continuous spinal anesthesia, a laparotomy was done through a right rectus incision. A greatly distended gall bladder and common duct were exposed. A mass which appeared movable was felt in the head of the pancreas. The distended gall bladder interfered with exposure; therefore it was drained of normal-colored bile. A radical resection in one stage was decided upon. The stomach was divided proximal to the pylorus and closed. The duodenum was freed and divided 5 cm. distal to the lesion. The common duct was isolated, ligated, and divided. The closure was reinforced by interrupted sutures of silk. The body of the pancreas was then bisected 3 cm. from the lesion. Two distended ducts were separately ligated and the pancreas was turned in with silk.

The head of the pancreas was markedly adherent to the portal vein and had to be freed from it by sharp dissection. The jejunum could not be brought in contact with the gall bladder without tension, probably because of the marked scoliosis, but as the distal end of the duodenum was readily available the author made an anastomosis between the gall bladder and the duodenum. Silk was used for the serosal layer and catgut for the mucosal, in all the anastomoses. Following this a routine retrocolic, posterior gastrojejunostomy was done. Two cigarette drains were placed next to the bisected pancreas and brought out through a stab wound. The peritoneum was closed with catgut, the anterior rectus sheath with catgut and tension sutures of wire, and the skin with wire. The patient received 500 cc. of blood and 800 cc. of normal saline solution on the table.

The pathological report was "adenocarcinoma of the pancreas."

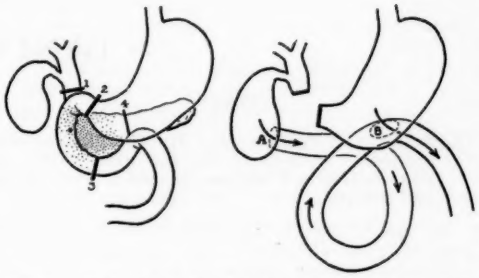


Fig. 1. Left, Schematic drawing showing points of division as described in the operative note.

Fig. 2. Schematic representation following anastomosis. The pancreas and transverse colon are not shown for the sake of clarity.

The postoperative course was smooth. Starting on the third postoperative day and lasting until the twelfth postoperative day, there was profuse drainage from the stab wound of what was assumed to be pancreatic juice. No bile was ever noted in this drainage. The patient was discharged from the hospital on her twenty-third postoperative day.

The author concludes that permanent cure of carcinoma of the head of the pancreas will follow the successful resections only rarely. The anatomic position of the pancreas adjacent to vital structures (portal vein) which cannot be sacrificed prevents one from doing a wide resection of the growth. However, life expectancy can be increased, as in this case, in spite of the fact that the pathologist found the tumor at the very edge of the resected tissue.

JOSEPH K. NARAT, M.D.

GYNECOLOGY

UTERUS

Chaffin, R. C.: Procidentia. The Chaffin Vaginal Subtotal Hysterectomy for the Cure of Fourth-Degree Prolapse; Review of Technique and Results. *Am. J. Surg.*, 1944, 66: 328.

The author prefers the Watkins-Wertheim interposition operation for the correction of cystocele associated with minor degrees of uterine prolapse. He describes an operation devised to remedy more severe grades of prolapse associated with uterine, bladder, and cul-de-sac protrusion. The cervix is treated with the Percy cautery if indicated. A supracervical hysterectomy is then performed by the vaginal route, and the severed ends of the round and broad ligaments are sutured into the lower posterior surface of the cervix or into the cul-de-sac itself. The retained cervix is sewn to the pubovaginal fascia to obliterate the opening through which the bladder protrudes and the operation is completed with a perineorrhaphy.

GEORGE BLINICK, M.D.

Macfarlane, C., Sturgis, M. C., and Fetterman, F. S.: The Value of Periodic Pelvic Examination in the Control of Cancer of the Uterus. *J. Am. M. Ass.*, 1944, 126: 877.

A group of presumably well women between thirty and eighty years of age volunteered to come for pelvic examination twice a year for five years to test the value of periodic pelvic examination in the control of cancer of the uterus. A total of 9,111 examinations have been made; 545 volunteers have completed the five-year period.

In the course of these 9,111 examinations, 4 early cancers of the cervix and 1 early cancer of the uterus were discovered. The patients were adequately treated. They remain well, 2 for six years, 2 for five years, and 1 for fifteen months after treatment.

Also in the course of the 9,111 examinations, 461 inflammatory lesions of the cervix were discovered. Two hundred of these have been treated and eliminated.

GEORGE BLINICK, M.D.

Ingraham, C. B., Black, W. C., and Rutledge, E. K.: The Relationship of Granulosa-Cell Tumors of the Ovary to Endometrial Carcinoma. *Am. J. Obst.*, 1944, 48: 760.

Granulosa and theca-cell tumors may be associated with such excessive and abnormal endometrial hyperplasia that a histological pattern indistinguishable from adenocarcinoma results.

In further investigation of this question, the authors studied a series of 6 hysterectomy specimens, including the ovaries, in corpus carcinoma, in order to determine whether or not hyperplasia of ovarian stroma, interstitial cells, or follicular lining cells was associated with carcinoma. This study showed no constant relationship, and it was found that the ovaries were either partially or completely atrophic in all instances. The amount of deeply basophilic mesodermal tissue present in the ovarian stroma and not demonstrably connected with follicular structures was variable, and while a considerable amount of this tissue was present in some cases, there was almost a total lack of it in others. A further series of 15 corpus cancers was studied for histological comparison with endometrial hyperplasia associated with granulosa-cell tumors.

Examination of such specimens provided an opportunity for comparison of the growth characteristics of corpus carcinoma and the condition of excessive proliferation caused by granulosa-cell tumor.

The most important features of corpus carcinoma are its progressive growth with continuous and irreversible proliferation, with invasion of the myometrium and establishment of metastases. Some of these features are lacking in many true carcinomas and in all reported cases of excessive hyperplasia, including the authors'.

Two additional cases of granulosa-cell tumor and 1 case of theca-cell tumor of the ovary associated with adenocarcinoma of the corpus uteri are reported.

EDWARD L. CORNELL, M.D.

Peralta Ramos, A. G., and Gramajo, G.: Immediate and Late Results of the Wertheim-Schauta Operation (Resultados immediatos y alejados de la operacion de Wertheim-Schauta). *Obst. gin. lat. amer.*, B. Air., 1944, 2: 766.

Genital prolapse is frequently accompanied by retrodeviation of the uterus. The operation for the correction of these conditions was formerly performed in two stages, a vaginal and an abdominal one. However, it has been found advantageous to suppress the abdominal stage and operate entirely through the vagina. The Wertheim-Schauta operation fulfills this requirement. It interposes the uterus between the bladder and the anterior wall of the vagina, which occludes the vagina and permits the uterus to act as a support for the bladder. The chief indication for the operation is found in cases of prolapse of the second degree with a large cystocele and incontinence of urine. It is a simple operation and easily accomplished under local anesthesia. The vaginal flora should be studied in determining its indications, and it should be supplemented by the local intraperitoneal use of a sulfonamide. It should be used only for women at or near the menopause as pregnancy under the anatomical conditions created by it is dangerous.

The authors give the histories of 28 patients on whom they have used this operation. Fourteen of them returned for later examination and, of these, 11, or 78.57 per cent, were permanently cured, while 3, or 21.43 per cent had a recurrence. It is a good

operation for genital prolapse provided it is performed on the proper indications. North American physicians call this "Watkins operation" as they claim that the first interposition operation was performed by Watkins in 1898.

Recurrences are generally caused by elongation of the cervix, and to prevent them Wagner recommends amputation of the cervix during the operation and Wertheim proposes fixing it to the uterosacral ligaments. AUDREY G. MORGAN, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

Rubin, I. C., Novak, J., and Squire, J. J.: Ovarian Fibromas and Theca-Cell Tumors; Report of 78 Cases, with Special Reference to the Production of Ascites and Hydrothorax (Meigs' Syndrome). *Am. J. Obst.*, 1944, 48: 601.

The first group of tumors, reported from 1928 to 1936, consists of 23 cases. In 7, the tumors were small, measuring at most 5 cm.; in 10 cases they were of medium size, from hen-egg to apple size; and in 5 cases they were large, bigger than an average-sized grapefruit. In 1 case there was no definite note as to size. Ascites was observed in 9 cases of this group. In 2 cases the amount of fluid was small, in 3 moderate, and in 4 considerable. In 6 cases with ascites, the tumors were of large size, and in 3 they were of medium size. In 7 cases, the tumors were edematous and, for the most part, cystic; in 2 cases they were hemorrhagic. Hydrothorax was found in only 1 case of the group. The pleural effusion was bilateral and much more pronounced on the right side than on the left. It was hemorrhagic, whereas the ascitic effusion was described as amber-colored. This unusual circumstance is not explained by the authors.

The second group of tumors consisted of 30 fibromas (including fibromyomas), 2 papillary fibroadenomas, and 23 theca-cell tumors. This fairly large group indicates incidentally that theca-cell tumors are not as rare as has been generally assumed. Three of the fibromas were large, 14 of medium size, and 13 small. There was a small amount of ascites in only 2 of the fibroma cases. The relative infrequent occurrence of ascites in this group is difficult to explain. In 1 of the 2 cases of papillary fibroadenoma a small amount of ascitic fluid was found at operation. Hydrothorax was not found in any of these 30 cases of ovarian fibroma.

Among the 23 cases of theca-cell tumors, ascites was noted 7 times. The abdominal effusion was extensive in 3 cases with large tumors. A hydrothorax on the right side was associated with the ascites in 1 case. In 4 cases with a moderate amount of ascitic fluid, the tumors were only of medium size, i.e., from that of a hen's egg to that of a grapefruit. In 6 cases with ascites, the new growths were edematous, and in 4 cases, cystic.

Ascites is not a frequent occurrence in ovarian fibromas if one considers all of the fibromas including the small ones.

Ascites, as well as the combination of ascites and hydrothorax (Meigs' syndrome), is also found in theca-cell tumors.

The ascitic fluid probably originates from the tumor itself. Geibel's observation on the oozing of fluid from an ovarian fibroma placed in a dry vessel should be verified. The conditions which may bring about a lymph congestion in the tumor should be studied by a thorough examination of the lymph and blood vessels in the tumor tissue, in the pedicle, and on its surface.

In every case of Meigs' syndrome, the specific gravity, the albumin and cell content, and the osmotic pressure of the ascitic and pleural effusions should be determined.

The anatomic routes by which fluid is transferred from the peritoneal into the pleural cavity are described. Living cells, cell debris, or chronic inflammatory changes of the peritoneum or of the pleura may block the connections between these two cavities.

The prevalence of pleural effusions on the right side can be explained by anatomic and physiological conditions, i.e., the better development of the diaphragmatic lymph channels, the higher position of the diaphragmatic dome, and the more intensive pumping action of the diaphragm on the right side.

A hydrothorax can best come about not only if the ascitic fluid is poor in colloids, and therefore can easily pass the diaphragm, but also if the absorption and deportation of the fluid is not rapid enough in the pleura to prevent its accumulation.

EDWARD L. CORNELL, M.D.

MISCELLANEOUS

Miller, H. E.: Deaths in Gynecology. *Am. J. Obst.*, 1944, 48: 824.

The general impression received from a study of 401 deaths (two-thirds of which were due to malignancy) is that, on the whole, the cases were well managed from the standpoint of the hospital, and that in the great majority of cases (particularly the malignancies), after due allowance is made for the speed and general hopelessness of such conditions as adenocarcinoma of the ovary, the patients were responsible for their own deaths. On the other hand, in perhaps 25 per cent of the cases with death from malignant disease the patients might have been given a chance of life; and in perhaps half with death from benign disease the outcome might have been different if the plan of management *outside as well as inside of the hospital* had been different in some or in all respects.

Ectopic pregnancy was the cause of the death of 15 patients, 9 of whom were not submitted to surgery. This is a truly startling situation, for of all emergency gynecological conditions, none responds more promptly and more satisfactorily to surgical therapy than ectopic pregnancy. Histories should be taken with much more care from every standpoint.

There should be less complacency about the risk in both uterine fibroids and pelvic inflammations. In this series, the responsibility for the cases in which there was an unwise estimation of the risk was about equally divided between the surgeon and the medical consultant.

In all surgical cases there could well be a more careful evaluation of the need for preoperative therapy, even when the patients seem fair risks and present only minimal deviations from the normal. Blood surveys should be carried out in all cases, and mild degrees of anemia, hypoproteinemia, urinary-tract disease, and hepatic dysfunction should be investigated.

There should be more alertness after operation to detect possible complications in their incipiency, more speed in instituting treatment when such complications are discovered, and a quicker resort to such measures as intestinal decompression, infusion, transfusion, and oxygen therapy when it is evident that less active measures are not achieving results.

More discretion should be employed in discharging patients in certain categories without adequate provision to bring them back if they do not return voluntarily as directed. A fair number of women with malignant disease in this series signed their own death warrants because, when they improved after irradiation which was well begun, they failed to return for more. Patients with pelvic inflammations who responded to bed rest often delayed likewise.

Patients with obvious abscesses, among whom the proportion of rupture was startlingly high, should be kept under observation in the hospita and should be operated on promptly when maximum improvement is evident, or when it is clear that no further improvement can be expected.

A more general use of total hysterectomy would automatically prevent the development of a certain proportion of cases of malignancy of the cervix.

It should never be forgotten that a patient with one disease, even if that disease is malignant, may have or develop another disease, even a malignant one, at the same time. Pelvic examination should be made a routine part of all physical examinations. A much higher "index of suspicion" of malignant disease, and especially of malignancy of the cervix, must be ingrained in medical students, interns, and residents. Interns and residents, in particular, must be imbued with the belief that not all instances of malignant disease are hopeless, an idea which a surprising number of them now seem to possess, and which results in an eager desire to clear the wards of such cases and to use the beds for other purposes. For frank errors of diagnosis and treatment we are responsible as individuals, and most of the preventable deaths from benign disease in this series fall into that classification.

As many of these cases show, the menopausal years are a period of particular danger in a woman's life because of the possible confusion between the expected irregularities of those years and the early symptoms of malignancy of the cervix. The solution would seem to lie in teaching women to submit to pelvic examination at regular intervals, whether or not they present symptoms.

EDWARD L. CORNELL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Ayre, J. E., and Kearns, P. J.: The Course of Pregnancy Following Total Ovarian Ablation. *Canad. M. Ass. J.* 1945, 52: 24.

The authors report a case of removal of an ovarian cyst in a patient two and one-half months pregnant whose other ovary had been previously removed. Following the operation from the sixty-third to the eighty-third day of pregnancy the urine pregnandiol readings were zero consistently, but they later increased to a high of 18.9. The pregnancy advanced normally until about five months, at which time it terminated spontaneously.

The period during which no pregnandiol was excreted probably represents the interval between the removal of the corpus luteum and the assumption of the function of hormone production by the placenta.

J. Robert Willson, M.D.

Williams, P. F., and Corbit, J. D.: An Analysis of 101 Fatalities from Ectopic Pregnancy. *Am. J. Obst.*, 1944, 48: 841.

In Philadelphia, among 2,204 ectopic gestations recorded by the hospital record librarians and the Coroner's office from 1931 to 1943, inclusive, there were 101 deaths, a mortality of 4.6 per cent.

This study presents a review of these fatalities and attempts to fix responsibility for the deaths, and to seek out the avoidable factors.

The responsibility has been found to be divided between the patient and her family, the referring physician, and the attending surgeon and his hospital staff. The avoidable factors have been found to include lack of education of the laity regarding early and adequate prenatal care; failure of the referring physician in recognizing the possibilities of differential diagnosis; failure on the part of the surgeon in diagnosis, and because of delay in operating, lack of transfusion, and poor choice of operative procedure.

Edward L. Cornell, M.D.

Crabtree, E. G.: The Use of the Sulfonamides in Pyelonephritis in Pregnancy. *J. Am. M. Ass.*, 1944, 126: 810.

According to the author sulfonamides have greatly modified the management of pyelonephritis in pregnancy. There is a definitely good effect which will make itself apparent promptly, as a rule. Patients who show signs and symptoms of pyelonephritis in pregnancy were given 2 gm. daily of sulfathiazole or sulfadiazine for six days. Sixty grains of sodium bicarbonate are also given three times daily while the patients are receiving the sulfa drugs. The fluid intake is between 2,500 and 3,000 cc. of water daily in addition to other fluids in the diet. This routine is followed with outpatients. Whenever patients are febrile they are hospitalized and the routine is more varied. Alkalization, forcing of fluids, and sulfathiazole are the basic items in the treatment of these patients.

All patients treated are relieved of symptoms although the patients are not all cured.

All obstetrical patients with pyelonephritis should be given a course of sulfonamide therapy and if the infection is not cleared up by this, they should be investigated for lesions of the urinary tract.

Cystoscopy is used more for diagnosis than for its therapeutic effect. Many patients are discharged from the hospital with infected urine and no symptoms. This may cause preventable gross damage to the urinary tract after long or repeated injuries. Therefore, it is important to realize that subsidence of symptoms following sulfonamide therapy does not mean cure. Patients should be checked carefully after pyelonephritis is diagnosed and followed up for sometime thereafter.

Harry Fields, M.D.

Finn, W. F.: Lymphogranuloma Venereum in Pregnancy. *Am. J. Obst.*, 1944, 48: 696.

The author briefly reviews 11 cases of lymphogranuloma venereum in pregnancy from the New York Lying-In Hospital. Patients with this disease are usually colored and they are almost invariably syphilitic; therefore when one encounters such a patient with a rare venereal disease one can almost infer that she will have a more common venereal disease. These patients are frequently anemic.

As to the type of delivery, a vaginal examination before the onset of labor or in early labor will give the most information. If there is marked perirectal fibrosis, soft-tissue masses, or fixation of the posterior vaginal wall, vaginal delivery will be fraught with difficulty and danger.

It is interesting to note that in both of the cases of rupture of the rectum, breech extraction was performed. Hence, when a breech presentation is found in a woman with a stricture of the rectum, external cephalic version should be attempted.

One colored patient (a para-iv and gravida-vi), after a three-hour first stage and a one-hour second stage of labor, developed a semicircular rupture of the uterus. She was operated upon and recovered. She also had syphilis. Edward L. Cornell, M.D.

LABOR AND ITS COMPLICATIONS

Morgan, J.: Report on 130 Consecutive Cases of Placenta Previa without Maternal Death. *J. Obst. Gyn. Brit. Empire*, 1944, 51: 509.

The author reports a consecutive series of 130 cases of placenta previa without a maternal mortality and with a fetal mortality of 22 per cent.

Of the 130 placentas, 32 were implanted centrally, 46 were marginal, and 52 were lateral. Treatment was as follows:

Central placenta previa (32 cases)	
Cesarean section	30
Application of Willett's forceps	1
Manual removal of the placenta before delivery of the infant when the patient was admitted fully dilated	1
Marginal placenta previa (46 cases)	
Cesarean section	15
Application of Willett's forceps	19
Plugging with the half-breech	3
Artificial rupture of the membranes	4
Manual delivery	1
Normal delivery	4
Lateral placenta previa (52 cases)	
Cesarean section	2
Application of Willett's forceps	16
Artificial rupture of the membranes	16
Normal delivery	18
Blood transfusions were required in 16 cases.	
The causes of fetal death were:	
Prematurity	20
Congenital atelectasis	4
Cerebral hemorrhage	1
Congenital defects	3

J. Robert Willson, M.D.

MISCELLANEOUS

Dempsey, E. W., and Wislocki, G. B.: Observations on Some Histochemical Reactions in the Human Placenta, with Special Reference to the Significance of the Lipoids, Glycogen, and Iron. *Endocrinology*, 1944, 35: 409.

The authors describe some interesting histochemical reactions in the placenta. These are concerned chiefly with lipoids, glycogen, and iron. The material for study consisted of 9 human placentas of various ages, the youngest coming from an embryo 3 mm. in length. Some of the placentas were fixed in various reagents for special cytological study, while others were studied fresh and unfixed.

The types of study included fluorescence studies, transillumination with ultraviolet rays, and birefringence with a polarizing microscope. The Schiff, or "plasmal," reaction of Feulgen and Voit was used to study aldehydelike compounds, and strong sulfuric acid was applied to fresh and formalin-fixed tissues to determine the localization of steroidlike substances. Best's carmine stain was utilized to locate glycogen. The oxidative systems of the placentas were studied by means of the application of "nadi" reagents and their ability to oxidize or reduce a series of indicator dyes.

The conclusions reached by these observers are that lipoids of the fetal placenta occur almost entirely as droplets in the syncytial trophoblast. These droplets contain steroidal substances. The cytotrophoblastic cell columns, cell islands, and cytotrophoblastic shell contain glycogen, especially during the early part of pregnancy. Similarly, a considerable amount of glycogen is present in the decidua in the first half of pregnancy. The authors suggest from their conclusions that glycogen deposition is associated with anaerobic conditions, and that through anaerobic breakdown, a mechanism for oxidative reactions of tissues in which the oxygen supply is deficient is produced. They also concluded that the syncytium of early placentas contained a considerable amount of iron, while in the later stages of pregnancy this amount is greatly reduced. These findings are interesting with regard to iron transport by the placenta. Harry Fields, M.D.

Avendaño, O.: Maternal Mortality from Obstetrical Causes in Chile (Sobre mortalidad materna por causas obstétricas en Chile). *Bol. Soc. chilena obst. gin.*, 1944, 9: 179.

The author gives tables which show the maternal mortality from obstetrical causes in Chile from 1915 to 1943. The causes of death are also tabulated and the statistics are compared with those of other countries. Part of the statistics were obtained from the Government Statistical Bureau and part from various hospitals, and attention is called to the causes for the differences in the government and hospital statistics. The author believes that the best way of calculating such statistics is to count the number of maternal deaths to every 10,000 infants born alive. The arguments for and against the various methods of computing statistics are set forth.

The author finds with regret that there has not been a decrease in the maternal mortality in Chile within this period comparable with that in other highly civilized countries. In the United States there has been a rapid decrease in maternal mortality since 1930. In England and Wales there has been some improvement in the last decade, while in Norway and the other Scandinavian countries the figure is very low.

He attempts to explain the backwardness of Chile in this respect. Chilean physicians know the most modern medical and surgical methods of management of delivery and the puerperium. However, the fault seems to lie in the fact that this knowledge and skill is not made available to the mass of the population. It is a social as well as a medical question. In the United States there is a learned society devoted entirely to the investigation of the causes of maternal mortality and a detailed study of each case of death, while in Chile there is no such activity. Chile should organize early and compulsory prenatal control, and pregnant women should be under medical observation and care from the beginning of pregnancy. Medical and scientific societies should accept the responsibility of bringing about better obstetrical care for the mass of the population.

In the discussion the facts were brought out that it is difficult to lower the maternal mortality until induced abortion with its high percentage of sepsis can be controlled, and also that the highest mortality in Chile is in the country districts where the skilled medical care of the cities is not available.

Audrey G. Morgan, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Darmady, E. M., Siddons, A. H. M., Corson, T. C., Langton, C. D., and Others: Traumatic Uremia; Reports on 8 Cases. *Lancet*, Lond., 1944, 247: 809.

Six fatal cases and 2 nonfatal cases of uremia which occurred in young soldiers a few days following injury by high-explosive missiles are reported. The injuries were severe but in themselves did not seem sufficient to cause death. All of the men developed oliguria, vomiting, and a raised blood urea. Many of them had a low blood pressure and were in clinical shock at one time during their illness. Pathological examination of the kidneys in 4 cases coming to autopsy revealed enlargement of the kidneys with histological evidence of tubular degeneration, interstitial edema, and rupture of the tubules into the venous spaces.

The similarity between the pathology of this syndrome and the "crush syndrome" is great. The renal changes are probably due to anoxia secondary to hypotension or vascular spasm, or both, and are probably not dué to "nephrotoxic" substances liberated from crushed tissues as there was little crushing present in these cases. These 6 fatalities represent one-third of the deaths in a group of 2,000 casualties which were observed in a transit air-evacuation hospital in northern France.

WILLIAM W. SCOTT, M.D.

Dean, A. L., and Abels, J. C.: Study by Newer Renal Function Tests in an Unusual Case of Hypertension following Irradiation of One Kidney and Relief of the Patient by Nephrectomy. *J. Urol.*, Balt., 1944, 52: 497.

The measurements of renal function commonly employed by urologists such as the determination of blood nonprotein nitrogen, and urinary concentration, and the dilution tests, do not always measure accurately the amount or nature of renal damage and provide still less information of the reserve capacity of the organs.

A case illustrative of the value of the newer renal function tests is presented. At the age of twenty years a woman complained of an abdominal mass of six weeks' duration. Except for the mass, physical and laboratory examinations were normal. Urograms were normal. Under a diagnosis of lymphosarcoma or Hodgkin's disease 3,000 roentgens were administered through anterior and posterior portals, and it was calculated that the kidney received 4,600 roentgens. The tumor disappeared completely, but seven years later the patient's blood pressure was 150/100, and when headaches began to appear it was found to be 184/125. Excretory urograms showed a shrunken left kidney with diminished function. The usual tests showed little impairment of the left renal function, but when the rate of glomerular filtration was measured by the mannitol clearance technique it was found that the left kidney cleared only 17 ml./min. The renal blood flow as determined by the sodium para-aminohippurate method was 410 ml./min. for the right and only 70 ml./min. for the left kidney. Maximum tubular secretion of this compound was shown to be 50 mgm./min. on the right side and 6 mgm./min. on the left side.

Following removal of an atrophied left kidney the blood pressure fell from 160–172/120–130 to 112–120/72–80 within one week. During the following fourteen months the blood pressure remained in this range and renal function tests showed slight improvement in the function of the remaining kidney. Vascular responses to cold and nitroglycerin, which were poor preoperatively, became normal, and the venous pressure and circulation times decreased to normal values following operation.

It is suggested that when it is important to determine the functional capacity of a kidney, use of the newer tests of renal function be made as the present function tests are frequently inaccurate and are not sufficiently sensitive to detect renal damage.

WILLIAM W. SCOTT, M.D.

Deming, C. L.: Acute and Chronic Symptoms and the Diagnosis of Movable Kidney. *Pennsylvania M. J.*, 1944, 48: 207.

Although mobility of the kidneys is normal, in some adult females it causes pain presumably because of temporary obstruction of the pelvis of the kidney. Pain, the most common symptom of pathologically movable kidneys, is usually referred to the corresponding costovertebral angle, although gastrointestinal complaints and nervous symptoms may predominate. In a certain proportion of the cases hydronephrosis is present, and impaired renal function and delayed emptying of the renal pelvis are the late effects of pathologically movable kidneys. Treatment of 200 selected cases by suspension of the kidney resulted in failure to relieve the symptoms in only 4 cases.

The author mentions the fact that the Kelly stitch operation and capsule-stripping operations for nephropexy should be avoided because of the danger of perinephritis and hypertension. The author's nephropexy consists of complete mobilization of the kidney, pelvis, and ureter, the kidney being placed in its correct position, and the anterior and posterior layers of the perinephric fascia being approximated with chromic mattress sutures to maintain the kidney in normal position. Nephropexy may be indicated following pyelolithotomy or plastic operations on the renal pelvis to maintain the normal position and emptying of the pelvis of the kidney.

DONALD F. MCDONALD, M.D.

Crabtree, E. G.: Leiomyoma of the Kidney Associated with Hemorrhagic Cyst. *J. Urol.*, Balt., 1944, 52: 480.

Tumors which arise from smooth muscle tissue and are situated beneath the true capsule of the kidney are usually small, multiple, benign fibromyomas and usually do not require surgical treatment. Myomas of the kidney have grown to larger size, produced symptoms, and assumed surgical significance in a very small number of reported cases. Of 8 reported cases of renal myomas of large size only 2 were histologically malignant. The benign myomas have a tendency toward cyst formation both in association with the tumor and within it. Of the 6 reported benign myomas 3 were accompanied by cyst formation, whereas the 2 malignant myomas lacked cysts. In the cyst wall, encrustation with cholesterin or calcium was the rule. Both benign and malignant tumors have been found well encapsulated within the renal capsule. Results of nephrectomy for renal myoma are good, no doubt because extension into the perirenal fat and veins does not occur. Of the 8 tumors recorded, 6 have been in women. The age incidence of renal myoma is from twenty-one to fifty-two years with 7 patients under thirty-nine years.

Two cases of renal myoma are presented. One was benign and occurred in a male aged thirty-nine years whose initial complaint was loin pain and who has remained well for six months. The other was malignant and occurred in a forty-three-year-old woman who complained of a left abdominal mass. Following nephrectomy it recurred in three years and was again removed; then it recurred in two years at which time further surgery was instituted.

In the first case the tumor was a thick-walled cyst 5 cm. in diameter, the wall of which contained calcification and whorls of smooth muscle and connective tissue without evidence of malignancy. In the second case the tumor was 16.5 cm. in diameter and was not cystic. Microscopic examination showed connective tissue, smooth-muscle cells, and numerous mitoses which led to the diagnosis of leiomyosarcoma.

Until greater familiarity with the clinical appearance of leiomyomas of the kidney is attained, pathological examination of the specimen removed by nephrectomy should be regarded as the only reliable method of establishing the malignancy or benignancy of the tumor.

WILLIAM W. SCOTT, M.D.

Sugarbaker, E. D.: An Application of Staging in the Removal of Difficult Wilms' Tumors. *Ann. Surg.*, 1944, 120: 901.

Mixed tumors of the kidney occur most frequently in infancy and early childhood; they are characterized by rapid growth to large size and early metastases to the lung and liver, and have a quickly fatal termination.

Roentgenotherapy either alone or as a preoperative adjunct is much inferior to immediate nephrectomy. A transperitoneal approach is desirable because it permits of the intact removal of the tumor and the perinephric fat within the fascia of Gerota. Another advantage of this approach is that it permits primary ligation of the renal pedicle before the tumor is disturbed, which is desirable because of demonstrable renal vein involvement in 45 per cent of the cases.

Operability of these tumors depends not only upon the presence of metastases but also upon the technical ability of the operator and the size and position of the tumor. Operability may be extended by dividing the operation into two stages to minimize the risk and to facilitate the excision of the bulky, very vascular tumor. Ligation of the pedicle of the kidney and mobilization of a portion of the tumor at the first stage permits of rapid excision with less bleeding at the second stage. The kidney and tumor should be removed intact with the perinephric fascia and fat and the overlying peritoneum.

A case of mixed tumor of the right kidney in a twelve-year-old boy in which a 1,760 gm. specimen was removed by the two-stage procedure described is presented in detail. The stages were six days apart, and the patient is in good condition two years after operation without evidence of recurrence.

DONALD F. MCDONALD, M.D.

McClelland, J. C.: Primary Carcinoma of the Ureter Treated by Excision and Anastomosis of the Cut Ends. *J. Urol.*, Balt., 1944, 52: 522.

A man, aged sixty-two, noticed two weeks before consultation that there was some blood in the urine after walking. The blood was intimately mixed with the urine, and he noticed a few small clots. There was no frequency, no pain, and no difficulty in urination. He gave a history of having passed 2 stones from his left ureter two years ago. There was an indefinite area of pain in the left lower quadrant, but none in the right lower quadrant.

Under local anesthesia a No. 24 F. cystoscope was introduced and clear urine was found in the bladder. The vesical mucosa throughout was pale pink in color and showed no stone, tumor, or foreign body. No intravesical enlargement of the prostate was present. The ureteral orifices were examined and no efflux was seen coming from either side. A catheter, passed up the left ureter, did not meet any obstruction. The right ureter was not catheterized as the patient had had his pain on the left side previously and the author suspected a recurrence of ureteral stone. The left pyelogram was negative for calculus or any abnormality in the pelvis or ureter.

An intravenous pyelogram showed a right hydronephrosis with a kinking of the upper ureter. The cystoscopic examination was repeated, and a stricture in the lower end of the right ureter, a kink at its upper end, and an incompletely filled hydronephrosis were found. A tentative diagnosis of new growth in the lower end of the right ureter was made and an exploration recommended.

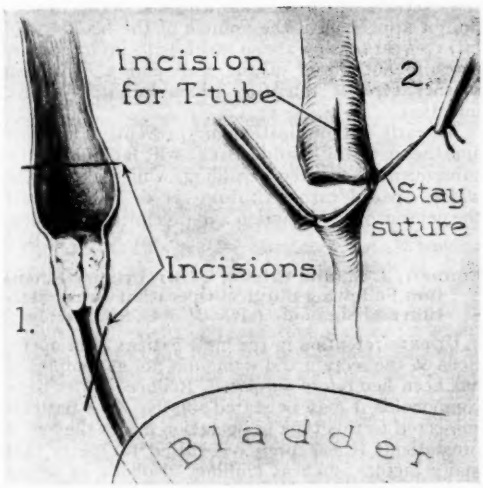


Fig. 1. *1*, Diagrammatic representation of ureter in section, showing growth and its lumen. Lines show areas where ureter was cut off. *2*, Stay sutures draw cut ends and ureter together and slit was made above to insert T-tube.

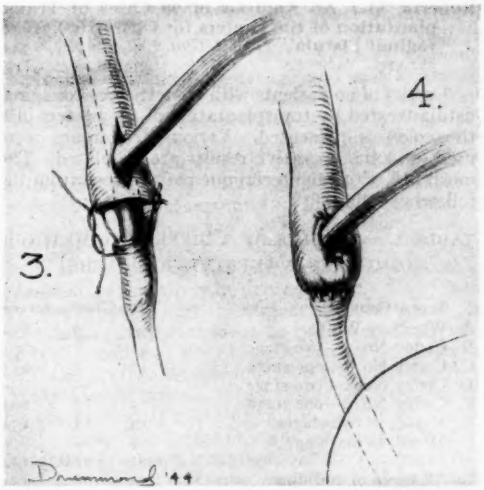


Fig. 2. *3* and *4*, Cut ends of ureter being approximated around T-tube with lower arm of T-tube extending into the lower ureter. Continuous suture of No. 0000 catgut was used after stay sutures were tied.

An incision, 10 inches in length, was made in the lower right quadrant of the abdomen, lateral to the rectus muscles, with the anterior superior spine in the middle of it, but 2 inches medial to it. The external oblique muscle was split in the direction of its fibers, while the internal oblique and transversalis muscles were cut and the ureter was exposed by pushing the peritoneum toward the midline. Just below the brim of the true pelvis the ureter showed a hard area which was discrete and not attached to any surrounding structures. The ureter immediately above the lump was quite dilated while the ureter below was not enlarged but the usual size. No evidence of any secondary tumors was seen. It was believed that this was a new growth, primary in the ureter, and the decision was made to excise it and join the 2 ends. The ureter was freed well up to and including the kink and plenty of slack ureter was present. Figure 1 (1) shows where the ureter was cut across in relationship to the growth. The upper portion was cut straight across and the lower portion cut on a slant. This was done in order to make the lower small ureter approximate more closely the size of the upper ureter. Figure 1 (2)—A slit was made in the upper portion, and a stay suture introduced to hold the edges together. In Figure 3 the small T-tube has been inserted and the lower end carried into the lower ureter. Several stay sutures were inserted after which a continuous suture was placed around the area of the anastomosis. When this portion of the operation was finished, it was believed that this should give a water-tight joint. No tension was present, but the ureter was quite slack. No. 0000 plain catgut was used to suture the ureter. The wound was closed in layers, a small tube being left down to the site of the anastomosis.

The wound was quite dry until the sixteenth day, when urine began to come around the tube and the patient had a low fever. This continued until his twenty-first day when the T-tube was withdrawn. The wound was wet a few hours only and completely dry in twenty-four hours and did not leak again.

The urine in the meantime had begun to show a good deal of pus. The prostatic secretion also contained a good deal of pus. A few prostatic massages and mandelic acid cleared the urine, the temperature came down, and the patient's condition was much improved.

Twenty-six days after the operation an attempt was made to catheterize the right ureter. Various catheters were used; these were blocked immediately at the ureteral orifice, and did not reach the site of the anastomosis. It was decided that edema was causing the obstruction and an attempt should be made at a later date to dilate the ureter.

Three and one-half months after the operation under spinal anesthesia the McCarthy panendoscope was used, and a large No. 12 bougie passed up the right ureter. This was obstructed at 5 cm., but went through with a little difficulty. It was withdrawn and a No. 11 Garceau catheter was passed. Good dilatation was obtained. Six weeks later dilatation was repeated under local anesthesia. Some slight obstruction was present but the ureter was dilated easily.

The pathological report was papillary carcinoma

JOSEPH K. NARAT, M.D.

Roberts, M.: An Analysis of 90 Cases of Transplantation of the Ureters for Obstetric Vesicovaginal Fistula. *J. Obst. Gyn. Brit. Empire*, 1944, 51: 519.

A series of 90 patients with obstetric vesicovaginal fistula treated by transplantation of the ureters into the colon is presented. Various techniques were used, and the operative results are tabulated. The mortality with each technique may be seen from the following table:

TABLE I.—RESULTS OF 2 DIFFERENT METHODS (OMITTING 2 ANESTHETIC DEATHS)

Type of Operation	Cases	Deaths	Mortality per cent
A. Winsbury-White	19	3	15.8
B. Coffey No. 1—two-stage	41	1	2.4
C. Coffey No. 1—one-stage	17	5	29.7
D. Coffey No. 2—two-stage	2	—	—
E. Coffey No. 2—one-stage	5	1	20.0
F. Mixed, in two stages	4	1	25.0
G. Mixed, in one stage	2	—	—
Average mortality			12.2
All types in one stage	24	6	25.0
All types in two stages	66	5	7.8

The author does not compare these techniques with repair of the fistulas, nor does he evaluate the more remote results. JAMES F. DONNELLY, M.D.

BLADDER, URETHRA, AND PENIS

Bellis, C. J.: Cystometry after Spinal Anesthesia. *Surgery*, 1944, 16: 896.

Ninety-four men without urological diseases and with ages ranging from eighteen to thirty-five were operated on under spinal anesthesia, and cystograms were made as soon as sensation below the level of anesthesia returned. The procedure followed in this investigation was detailed and an illustration thereof was published in the article.

Controlled determinations were made on 5 persons who had been given intravenous sodium-pentothal anesthesia for very short operations. The results showed that in the spinal-anesthesia group the intravesical tension increased slowly as the bladder was distended with fluid. The strong rhythmic contractions indicated by fluctuations in the manometer column, coincident with the desire to void, occurred at greater volumes and at higher pressures than in the controls.

Since the stretch reflex for the bladder is in the sacral cord, it is not surprising that residual vesical effects are found after the use of spinal anesthesia.

A discussion of the results obtained included the anatomy of the nervous supply to the bladder in relation to micturition. Spinal anesthesia is considered to establish temporarily a type of neurogenic vesical dysfunction probably due to the anesthetic agent. The bladder wall remains somewhat insensitive to its distending contents, and although the expulsive force of the detrusor muscle may actually not be diminished, the normal strong reflex vesical contractions which coincide with the desire to void do not appear until the volume of the bladder and intravesical tension are so great as to invite further pressure anesthesia of the wall and a continued sensory type of retention which initiates urinary infection.

An early catheterization, by preventing pressure anesthesia of the bladder wall, will facilitate early subsequent spontaneous voiding, while delayed and widely spaced catheterization serves to aggravate the neurogenic dysfunction and precipitate infection.

MARY KARP, M.D.

Emmett, J. L., and Cristol, D. S.: Urinary Retention Following Surgical Operation on the Rectum and Sigmoid. *J. Am. M. Ass.*, 1944, 126: 1077.

Urinary retention in the male patient after operations on the rectum and sigmoid is not as complex as has been heretofore supposed. Reduced to its basic components it may be stated simply. Most patients subjected to this type of operation are in the age of prostatism. It has been recognized for years that many factors, such as chilling, alcoholic or sexual excess, overeating, or surgical operations on other parts of the body, will precipitate urinary retention in such cases. Trauma to the prostate and urethra plus the removal of the supporting structures around the base of the bladder (such as occurs after posterior resection or combined abdominoperineal resection) furnishes an ideal situation for the bladder to "decompensate" and become unable to expel urine through a moderately obstructed vesical neck.

Instead of an attempt to increase the vesical tone (which is impossible by any means available at present), the rational procedure is to weaken the vesical neck and obviate the imbalance that exists between the detrusor muscle and the vesical neck. This can be easily accomplished by transurethral prostatic resection and will completely and quickly relieve nearly all patients suffering from this annoying condition. To avoid an unnecessary operation it is probably best to allow the patient a period of at least three weeks after the intestinal operation to regain his vesical function before transurethral resection is advised.

Barry, H. C.: Traumatic Rupture of the Urethra and Bladder. *Austral. N. Zealand J. Surg.*, 1944, 14: 104.

Rupture of the lower portion of the urinary tract, although relatively rare, is, nonetheless, important because early adequate treatment may avert a serious or undesirable outcome. Traumatic lesions of the lower urinary tract may be classified into three main groups: namely, (1) ruptures of the anterior urethra, complete or incomplete; (2) rupture of the posterior urethra, complete or incomplete; and (3) rupture of the bladder, extraperitoneal or intraperitoneal. The anterior urethra is ruptured by direct violence, and usually it is the bulb which is crushed against the pubic arch. The lesion is often diffuse and the periurethral tissues are pulped. Rupture of

the posterior urethra is associated with a fractured pelvis and is caused by indirect violence. The lesion is more circumscribed, but there is often wide separation. Traumatic rupture of the bladder is usually a complication of a fractured pelvis, but it may follow direct trauma to a distended bladder. Although penetrating injuries due to missiles of war will not fit into this classification, the principles of diagnosis and treatment are similar.

Rupture of the anterior urethra commonly follows a fall astride or a blow to the perineum in the male. The presenting signs are bleeding from the meatus, bruising in the perineum, and retention of urine. Shock is seldom severe. Catheterization is unnecessary for diagnosis. In typical cases the spasm of the sphincter prevents extravasation of urine for several hours. Unless the injury is at the distal end of the penis and the patient is able to void satisfactorily early suprapubic cystotomy is indicated. In many cases this is all that is necessary, but when perineal hematoma is present or in late cases with extravasation of urine, perineal drainage must be established. Perineal incision also permits of inspection of the urethra and suture of the divided ends. If the tissues are edematous and the urethra cannot be united without tension, only the roof of the urethra should be sutured. Early suture is not essential provided diversion of the urine is adequate. Suprapubic drainage must be maintained until the perineum is healed and any stricture is fully dilated. An indwelling urethral catheter, except when the edema has subsided and the wound is healing, is contraindicated by the danger of infection and increasing stricture formation. Regular dilatation of the urethra following healing of the wound must be carried out in some cases for a few months, and in others for life. Complications depend on the residual urethral stricture and its sequelae-periurethral abscess, urinary fistulas, urinary infection and calculus formation, chordee, sterility, and impotence.

Rupture of the lower urinary tract occurs as a complication of a fractured pelvis in probably less than 5 per cent of cases. It depends upon the site of fracture and the degree of displacement of fragments. Rupture of the lower urinary tract must always be suspected when separation of the symphysis or fracture of the pubic rami is present and especially in cases of complete fracture dislocation of the pelvic girdle. The urethra may be torn where it is held fixed by the membranous sphincter and either the bladder or urethra may be pierced by sharp fragments of bone. When the pelvis is laterally compressed and its anteroposterior diameter increased the puboprostatic ligaments may be torn, and as blood and urine accumulate in the prevesical space the bladder and prostate may be rotated upward and backward until there is often a gap of an inch or more between the torn ends of the urethra. In neglected cases the bladder may become anchored in its new position and late attempts at restoration may be fruitless. In these types of rupture the injury is often rapidly fatal or the patient is in such severe shock that restorative measures must be instituted immediately to preserve life. Reduction of the displaced fragments of the fractured pelvis prevents further shock and hemorrhage and may bring together the torn ends of the urethra. Temporary immobilization of the pelvis by a pelvic sling until operative measures to drain the bladder and restore the urethra are instituted is indicated. Diagnosis of intrapelvic rupture is established by the presence of suprapubic tenderness and dullness, retention of urine, bleeding from the meatus, and dislocation of the prostate upward. At this stage intrapelvic rupture of the urethra and extraperitoneal rupture of the bladder can rarely be distinguished. When there is doubt expectant treatment should never be adopted. A catheter must be passed and only if a normal amount of clear bloodless urine is withdrawn can the urethra and bladder be considered intact. When bloody urine is obtained the catheter may lie in the prevesical space or in the peritoneal cavity, and suprapubic cystotomy and exploration are indicated. Accessory investigations such as retrograde and excretion cystograms, and injection and withdrawal of known quantities of solution are uncertain and unnecessary and they waste time. At the time of suprapubic cystotomy a urethral catheter is passed retrogradely. If it passes into the bladder it is removed, a suprapubic catheter is left in the bladder and the prevesical space is drained. When the membranous urethra is completely torn the catheter will pass into the prevesical space. A sound may be introduced into the bladder by manipulation and an indwelling catheter splinting the urethra is withdrawn. If there is a tendency for the displacement of the bladder to persist, traction on a Foley type of catheter may be used to exert a constant pull on the bladder neck. Here, also, an indwelling splinting catheter is undesirable, but the soft parts must be kept in position at all cost. Direct suture of the membranous urethra, although theoretically the most desirable treatment, is attended by an increased risk to an already shocked patient. Late attempts at restoration of inadequately treated ruptured membranous urethras usually are unsuccessful and incontinence is usual.

Rupture of the bladder occurs as a complication of a fractured pelvis or following direct trauma to a distended bladder. About two-thirds of the ruptures are intraperitoneal and the mortality in these cases is about 50 per cent, depending also upon the severity of the concomittant injuries and the time elapsed between rupture and drainage of the bladder. In gunshot wounds, especially of the buttocks, in fractures of the pelvis, or when there has been a blow to the abdomen (especially in an alcoholic), the possibility of rupture of the bladder must be investigated by catheterization. If clear bloodless urine is not obtained the patient must be operated upon immediately. A suprapubic incision having been made, an extraperitoneal rupture is obvious by the widespread extravasation of blood and urine. Cystotomy is performed and the bladder is explored to exclude

any intraperitoneal lesion. If there is doubt the peritoneum may be opened and closed immediately if no free fluid is present. The prevesical space should be drained. If there is no extraperitoneal rupture the peritoneum is opened, the anterior wall of the bladder is opened extraperitoneally for drainage and the rent in the bladder is repaired. The peritoneal cavity is drained for twenty-four hours, the prevesical space a little longer, and the cystostomy is maintained for two weeks. In gunshot wounds, injury to other viscera must be excluded. WILLIAM W. SCOTT, M.D.

Taylor, J. A.: Penile Horn. *J. Urol.*, Balt., 1944, 52: 611.

Cutaneous horn, according to Ewing, is a peculiar form of cutaneous wart marked by excessive and progressive keratosis. These horns may appear anywhere on the skin of the body and are infrequently found on the penis. When found on the penis they are usually on the glans and may be single or multiple.

In view of the fact that these horns grow on a wart or acanthoma and are merely a progression of the keratosis already present in these two conditions, then it would seem that they are the result of prolonged irritation usually from a long prepuce.

Keratosis is a general term applied to pathological epidermoid proliferations, and the importance of keratosis as a precursor of cancer cannot be overestimated.

The author's patient was a thirty-five-year-old German male. His mother and father had both died of cancer. There was no relevant past history. His present illness began in Germany three years before when he noticed a small wart on the left aspect of his glans penis. The prepuce was adherent to the glans so a circumcision was performed, and the wart was excised. It recurred promptly and grew until it was again removed in March, 1939, in this country. On admission it had recurred and the patient presented a warty growth 1 cm. in diameter on the distal lateral aspect of the glans penis. General physical examination was essentially negative.

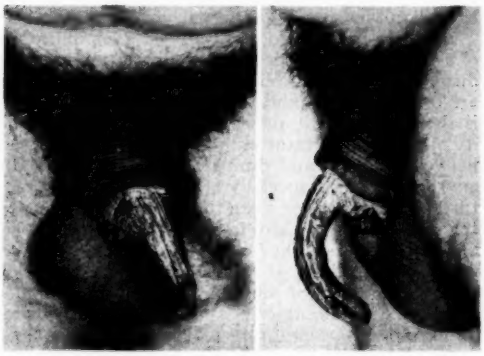


Fig. 1. Firm, hornlike growth from the penis.

Under low spinal anesthesia, the warty growth was excised with the electrosurgical knife. The pathological report read as follows: "Macroscopically, the specimen consists of a wedgeshaped piece of tissue 12 mm. long which has the appearance of a verruca. Microscopically, sections through the tissue show the growth to be composed of broad papillary masses of squamous epithelium with a few pearls but consisting largely of prickle cells. The basal layer is hypertrophic, and there are many mitotic figures. The tumor is growing in a papillary manner but with long extension of cells into a very vascular stroma. The type of cells and the manner of growth are more extensive than occurs in a papilloma, and the growth should be considered an epithelioma, but being highly differentiated and not showing deep infiltration with single cells, it is a Group I."

The patient was readmitted to the hospital in October, 1940, eleven months later, with a recurrence of verrucous growths extending to the coronal sulcus. Under low spinal anesthesia the growths were widely excised with the electrosurgical knife. This time examination of the specimen, macroscopically, showed a tumor of the penis in several portions, the largest 1½ by 8/10 cm. in size.

The patient was readmitted to the hospital in July, 1943, saying that several weeks after discharge, a small wart appeared and that one month later a horn began to grow out from this wart. It had grown steadily and at present was slightly over 3 inches in length. Under low spinal anesthesia the horn was removed with the electrosurgical knife, a deep wedge being cut into the glans.

The specimen consisted of a firm hornlike growth from the penis 9 cm. long by 3 by 2 cm. at the base and 1 cm. thick at the rounded tip (Fig. 1). On section, the base showed papillary outgrowths from the underlying derma. The line of the base was even and there did not appear to be any outgrowth. There was an additional portion from the base of the growth. On section, it showed epithelium from 4 to 7 mm. thick with vertical striation on one surface, and beneath this, a fibrous base. Microscopic sections through the base of the growth showed it to be composed of very long strands of hypertrophic squamous epithelium with many anaplastic changes and pearl formation in the deepest portion.

JOHN A. LOEF, M.D.

GENITAL ORGANS

Bumpus, H. C., Jr., Massey, B. D., and Nation, E. F.: Experience with Orchectomy for Carcinoma of the Prostate. *J. Am. Med. Ass.*, 1945, 127: 67.

The results obtained with bilateral orchectomy in 25 patients with carcinoma of the prostate are here reported. All of these persons, with 1 exception, showed decided improvement following the operation. Such improvement included such changes as increased vigor, strength, weight, and appetite, a

sense of well-being, cessation of pain, and diminished urinary difficulties.

The majority of these patients, although not all of them, were given diethylstilbestrol in doses ranging from 1 to 3 mgm. daily following orchectomy, and 13 had a transurethral prostatic resection in addition to the castration. The condition of the patient which was not improved remained about the same for six weeks before it began to grow worse; however, the patient was still alive thirteen months after the orchectomy, the metastases progressing and his health failing. (No case histories are appended.)

In the discussion of the results, all of these cases are divided into three groups: (1) 4 patients operated upon two years ago or more; (2) 11 patients operated upon between one and two years ago; and (3) 10 patients operated upon within the past year. Three of the first group cited are alive and well—1 patient at thirty months after orchectomy. One of the 3 had extensive pulmonary metastases which receded after the operation. The fourth is failing rapidly twenty-nine months after operation. Of the second group, 5 are dead, 4 are well, and 1 had a relapse after twelve months of relief. All of the patients in the third group are free of symptoms which indicate advancing malignancy.

There was considerable variation in the length of time required for softening of the prostate after orchectomy and the administration of diethylstilbestrol. There seemed to be no correlation between the length of the interval and the grade of malignancy.

In concluding the authors stress the fact that since 40 per cent of their patients who have been observed for a year or more following orchectomy have had a recurrence of symptoms, it is anticipated that all will eventually have a relapse. It remains, therefore, to regulate better our use of orchectomy or of the estrogens; it should be delayed probably until symptoms of an advanced malignant condition are manifest, then either method should be used separately, or in succession, rather than simultaneously.

The authors desire to call particular attention to a remarkable transformation in the patient's state of mind and personal habits (from a slovenly, apathetic habitus, to that of neatness, alertness, and interest in his surroundings) which occurred in a striking manner in one of these individuals, and which was more or less manifested by all the patients, immediately following the operation of bilateral orchectomy. This personality transformation is believed not to have been reported previously in the medical literature. JOHN W. BRENNAN, M.D.

Emmett, J. L., and Greene, L. F.: Bilateral Orchectomy for Carcinoma of the Prostate Gland. *J. Am. M. Ass.*, 1945, 127: 63.

The indication for bilateral orchectomy is carcinoma of the prostate with metastasis. Bilateral orchectomy is especially efficacious when the metastatic growths have given rise to symptoms. The period of relief following orchectomy varies from months to years, but whether any patients will remain permanently relieved seems extremely doubtful. Apparently the large majority of patients have a recurrence of symptoms within a year. Whether or not "prophylactic" orchectomy (done in the early stages of the disease before metastasis has appeared) measurably influences the course of the disease is not yet known. This problem cannot be settled until more time has elapsed and a larger series of cases in which "prophylactic" orchectomy has been performed has been studied. Until this problem has been definitely settled, the present practice of the authors is to advise orchectomy primarily for patients suffering from metastasis for the relief of metastatic symptoms. Results to date suggest that when orchectomy is performed in conjunction with transurethral resection the frequency of recurrent obstructive symptoms requiring subsequent prostatic resection is reduced; furthermore, if such symptoms do appear, the time interval between resections is increased.

The authors are also treating a group of patients who do not show evidence of metastasis with estrogens after transurethral resection to see if the course of the disease can be appreciably altered over a substantial period. They are interested to know if preliminary estrogenic therapy in such cases will tend to nullify the palliative effects of castration if the latter should become necessary for the control of symptoms later on.

Nesbit, R. M., Pazzos, R., and Cummings, R. H.: The Treatment of Prostatic Carcinoma by Castration and by the Administration of Estrogenic Hormone. *J. Urol.*, Balt., 1944, 52: 570.

The authors compare the results of castration in a series of 75 cases of prostatic cancer from six months to two years after operation with the results in a parallel series of 50 cases treated by the administration of 1 mgm. of diethylstilbestrol daily over periods of from six to thirty-five months.

In both series the relief of pain and the increase in weight have been striking. Complete relief of pain resulted in 64 per cent of the cases subjected to orchectomy as opposed to 56 per cent of the stilbestrol-treated cases. Weight gain was better in the stilbestrol series (78 per cent and 72 per cent respectively). Relief of partial urinary obstruction was greater in the orchectomy cases (86 per cent compared with 65 per cent). This would suggest that regression of the carcinoma was more complete following orchectomy. Following orchectomy, 85 per cent of the carcinomas decreased in size and 15 per cent became softer as judged by rectal examination. The comparable results with stilbestrol were: decrease in size in 33 per cent and softening in 16 per cent. In no castration case was the lesion observed to enlarge or fail to change in consistency or size, whereas in the stilbestrol series increase in size occurred in 12 per cent and no change was observed in 39 per cent of the cases. Metastases

regressed in 33 per cent of the castration cases, whereas in no case given stilbestrol did the metastases regress. Increase in the number and size of the metastases occurred in 67 per cent of the castrated patients and in only 38 per cent of those receiving estrogen. Deaths in the castration series amounted to 7 per cent, and in the estrogen series, to 8 per cent. Favorable responses occurred in 73 per cent and 80 per cent, respectively, and whereas there were no immediate failures in the stilbestrol group, 7 per cent of the castrated patients failed to derive any immediate benefit from the operation.

One case is presented in which the serum acid phosphatase failed to increase coincidentally with roentgenographical and clinical progression of the disease. Histopathological examination in this case revealed an abundance of acid phosphatase in the metastases.

The authors conclude that the acid-phosphatase level of the serum is an unreliable index of metastatic carcinogenic activity. In summary, they advise that although there is little difference in subjective response to the two forms of treatment, orchectomy results in greater objective regression in the primary tumor and metastases. Neither form of treatment affords prophylaxis against the development of or increase in metastases. Pain in postcastration cases can often be relieved by estrogen administration.

DONALD F. MCDONALD, M.D.

Barringer, B. S.: The Prognosis in Teratoma Testis. *J. Urol.*, Balt., 1944, 52: 578.

The vast amount of clinical and pathological material available to the author for study in the past twenty-eight years at the Memorial Hospital, New York City, is the basis for the present report.

The preoperative diagnosis of testis tumor, with the exception of those rare choriomas which produce high titers of urinary gonadotropins, is uncertain. The prognosis is not altered by preoperative irradiation of the testis. A review of 69 living patients showed that 80 per cent of the tumors were seminomas and 17 per cent were adenocarcinomas. There was 1 case of spindle-cell sarcoma and 1 of adult cystic teratoma. There were no cases of chorioma.

In the case of a patient with a testicular tumor, there is a large chance that he has a seminoma and a slight chance that he has an adenocarcinoma. There is only a remote chance that he has a chorioma or a nonmalignant tumor. Of 55 patients with seminoma, 56 per cent were well for five years or more, but of these, 29 per cent had metastases. In the group with adenocarcinoma, 83 per cent were well as long as five years, 40 per cent with metastases. While the testicular seminoma is much more radiosensitive than the adenocarcinoma, surprisingly few patients with metastasizing seminoma survive five years, while a relatively high percentage of patients with metastasizing adenocarcinoma survive more than five years.

The lymphatics of the spermatic cord are rarely invaded by testicular tumor although metastases to the lymph nodes pass through them. The prognosis is grave if metastases can be demonstrated in the cord, the supraclavicular nodes, the abdomen, the lungs, or the periprostatic lymphatics.

Autopsy material in 37 cases showed regional node involvement as follows: inguinal, 10.8 per cent; pelvic and iliac, 37.9 per cent; lumbar, 54 per cent; celiac, 56.8 per cent; mesenteric, 18.9 per cent; mediastinal, 48.7 per cent; bronchial, 35 per cent; and cervical, 35.2 per cent. Metastasis to the inguinal nodes is rare unless the tumor perforates the tunica or capsule of the testis. In many cases the center of the metastatic nodules or nodes were broken down and hemorrhagic, and in 5 cases there was hemoperitoneum. Intracranial metastases occurred in 16.2 per cent of the cases, but examinations of the brain were made in less than half of the cases on which autopsies were made. Pulmonary involvement was present in 78.3 per cent of the cases, and 55 per cent of these had also mediastinal node involvement; the pleura was involved in 37.9 per cent of the cases. In 75.8 per cent of the patients with pulmonary involvement, the liver too was involved. The involvement of the liver, being hematogenous, is unrelated to that of the testis. The spleen, diaphragm, pancreas, kidneys, adrenal glands, gastrointestinal tract, and skeleton were less frequently involved. Retroperitoneal involvement was found in 58.8 per cent of the cases, and in 33⅓ per cent of these the condition was bilateral.

In conclusion, the author advises concentration on the seminoma and the adenocarcinoma. Irradiation should be bilateral because the condition is bilateral in 72 per cent of the cases. Lung metastasis has a poor prognosis because liver involvement is present in 75 per cent of the cases. More extensive resection of the spermatic cord is advocated. The Chevassu-Hinman operation yields poor results in malignancy of the testis, which condition should be treated by orchectomy and irradiation.

DONALD F. MCDONALD, M.D.

MISCELLANEOUS

Keshin, J. G., and Pinck, B. D.: Factors in Male Sterility. A Critical Review of 135 Cases. *Am. J. Surg.*, 1944, 66: 346.

The present study was directed primarily to cases of male infertility not associated with obvious abnormalities such as hypospadias, cryptorchidism, and abnormal attachment of the epididymis to the testis. This study included a careful medical history with emphasis upon endocrinological and sexual factors, physical examination, and, when necessary, cystoscopy and catheterization of the ejaculatory ducts. Laboratory and x-ray examinations were made as indicated. At least two semen specimens were obtained by withdrawal and ejaculation into a glass container after five days' abstinence, and examined within an hour or two for motility, volume, count, mucolysis, and differential morphology. The criteria of morphology were those of Pollak and Joel,

and the motility was expressed in per cent as the ratio to nonmotile forms which lie in one-quarter of the microscopic field through an Ehrlich ocular screen. The total sperm count was determined in the counting chamber with 4 per cent boric acid, and 1 per cent phenol as a diluent. A histological study of a seminal smear stained with MacNeal tetrachrome stain was made. The normal values were: motility, 80 per cent after two hours; sperm count, from 60 to 120 million per cubic centimeter; and morphology, less than 30 per cent of abnormal forms.

A detailed analysis of 135 consecutive cases of sterile marriages indicated that the greatest correlation existed between a decreased sperm count and an increased per cent of abnormal forms and infertility. Motility and viability did not appear important. In only 32 per cent of the 135 sterile marriages were the semen analyses normal. In 25 per cent of the cases there was a decreased sperm count, an increased number of abnormal spermatozoa, and usually a decreased motility. The authors believe it is in this group of cases that endocrinological factors are responsible for sterility, and that testicular biopsy should be performed. In 25 per cent of the cases a normal sperm count was associated with a high percentage of abnormal forms, and it is in this group that the casual observer may pronounce a semen specimen normal unless special morphological studies are performed routinely. The etiology in this group is often obscure, but endocrine deficiency, foci of infection, exposure to x-rays, or dietary deficiency must be considered. Semen analyses by 2 roentgenologists showed normal counts and motility, but there was a shift to the immature types of spermatozoa among the abnormal forms present—probably the result of stimulation of spermatogenesis. Azoospermia was present in 24 (18 per cent) of the 135 cases. Among these 24, 10 patients had obstruction of the genital pathways due to past epididymitis, and 14 had defective spermatogenesis. Of those with defective spermatogenesis, 3 had had mumps orchitis, 1 had a history of seminoma with x-ray therapy, and 3 were found to have endocrine dysfunction. In only 1 case was improvement noted upon treatment with thyroid, corticosterone, and gonadogen; after two years of therapy impregnation was successful.

Treatment in cases of definite endocrine deficiency often was attended by dramatic results. However, these cases were few. When hypothyroidism was present, thyroid medication gave good results. Gonadotropins were ineffective. Vitamin B_1, B complex, and vitamin E were given in large doses, alone and with gonadotropins, but with no effect. Treatment of foci of infection was followed in some cases by improvement in the semen. In cases with excessive numbers of spermatozoa and an inordinate number of abnormal forms of the immature type, testosterone propionate (10 mgm. twice a week) caused a decrease in the total number and percentage of abnormal spermatozoa. Epididymovasotomy in cases of obstructive aspermia was unsuccessful. The authors comment that their results in five years in 135 cases are discouraging, as pregnancy resulted in only 11 per cent of the entire series.

The authors conclude that endocrine therapy plays a limited role in most cases of male sterility.

DONALD F. MCDONALD, M.D.

Usher, G. S., and Cowan, H.: Venereal Diseases Among the Migrant Farm Laborers of New Jersey. *J. M. Soc. N. Jersey*, 1945, 42: 11.

1. Of about 2,800 migrant farm workers in the potato-growing section of New Jersey, 756 were examined for venereal diseases. The examinations included blood tests and inspection for lesions and for gonorrhea. The women received routine gonococcus cultures.

2. The venereal disease rate was found to be very high, especially in women from fifteen to twenty-four years of age. In the latter group 6.3 per cent of those examined were found to have darkfield positive lesions of early syphilis, and 30.6 per cent were found to have gonorrhea.

3. Most of these infections were "imported" to New Jersey. The hazard to the areas through which these people travel and to the people of New Jersey is pointed out.

4. The living conditions of these workers are favorable to the spread of the diseases. These conditions urgently need correction.

5. Routine medical examination of *all* migrant workers and prompt application of rapid treatment methods are needed. Legislation to require such examinations and perhaps enforcement of the Interstate Quarantine Law would be helpful.

JOHN A. LOEF, M.D.

Exley, M.: Penicillin Treatment of Sulfonamide-Resistant Gonorrhea with Results of Multiple and Single Injection Methods. *J. Urol.*, Balt., 1944, 52: 626.

Two hundred and fifty-one cases of sulfonamide-resistant gonorrhea were treated with varying amounts of penicillin.

The dosage, varying from 41,300 to 125,000 Oxford units, was administered by intramuscular injections.

The result of the asymptomatic cure by means of the single injection treatment is dramatic. The amount of penicillin used should be at least 80,000 Oxford units. The absorption-elimination time is short, and this method may later be found to be more efficacious in previously untreated gonorrheal urethritis.

Excess dilution is frowned upon for the intramuscular treatment. This not only causes needless pain at the site of the injection, but also a more rapid rate of absorption. In another series being treated at present and to be published later, this has been found to be true.

There were only 5 cases with toxic manifestations in this series; all were transient and minimal in nature.

The follow-up examinations on the armed-service cases comprising 77 per cent of this series, have all been negative by culture and smear. The follow-up of the merchant service has not been as satisfactory, but the total average time of examination in both groups was thirty-one and two-tenth days. An average of 2.8 examinations have been made after the discharge of the patient from the hospital.

The average time for the cultures to become negative in all groups was twenty-one and one-tenth hours. The change may have occurred earlier but it was inexpedient to make tests at more frequent intervals.

Although the number of cases in this series is small, the use of penicillin is a gratifying addition to the curative armamentarium in the treatment of epididymitis associated with gonorrheal urethritis.

The combined use of hyperpyrexia and chemotherapy has yielded satisfactory results. There are still cases of failure in which this type of treatment will have to be utilized. The hospitalization time has been drastically reduced by the advent and substitution of penicillin.

An evaluation of the treatment from the results obtained, leads the authors to believe that certain methods used in this series are the most satisfactory. They are inclined toward the multiple-injection treatment, their preference being either 2 injections of 50,000 Oxford units for a total of 100,000 Oxford units, or 5 injections for a total of 80,000 Oxford units. At the present time they are running a larger series of the latter group.

The total treatment period has been reduced to below nine hours by means of the multiple injection method.

The total dosage of penicillin has been reduced.

From the observations made it does not seem desirable nor expedient, at this time, to recommend the one-day ambulatory treatment until further clinical studies have been made.

JOHN A. LOEF, M.D.

Bosworth, N. L., Riba, L. W., and Schmidlapp, C. J.: Two Hundred and Thirty-Three Cases of Sulfa-Resistant Gonorrhea Treated with 50,000 Units of Penicillin. *J. Urol.*, Balt., 1944, 52: 631.

Fifty thousand units of penicillin is an insufficient dosage to clear the average male gonorrheal infection; the results are failures in 23 per cent of the cases treated by this dosage.

A high incidence of positive and doubtful smears occurs during the first fourteen post-treatment days, but this indicates neither penicillin success nor failure. Positive smears and cultures usually indicate failure of cure.

Treatment with 100,000 units will clear the majority (85 per cent) of the 50,000-unit failures.

Hyperpyrexia and 100,000 intravenous units of penicillin will clear 30 per cent of the apparent penicillin-resistant gonorrheal infections. With an increase of penicillin supply, larger doses may be indicated during fever treatment.

Gonococcus carriers may also be produced with penicillin therapy, particularly when insufficient dosages are given.

One hundred and sixty thousand units of penicillin administered intramuscularly will result in the highest percentage (98 per cent) of clinical cures in the present-day treatment of sulfonamide-resistant gonorrheal infections.

Patients with complications should have correspondingly larger doses.

Penicillin is an excellent gonococcal bacteriostatic. The clinical cure occurs as a result of the host's defense mechanism provided it is not disturbed by "too much interference." JOHN A. LOEF, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Boger, W. P.: Pneumococcic Arthritis. Report of a Case of So-Called Primary Pneumococcic Arthritis. *J. Am. M. Ass.*, 1944, 126: 1062.

Pneumococcic arthritis should be regarded as the result of a septicemia.

A case of pneumococcic arthritis is presented in which no infection other than that in the knee could be demonstrated. A negro woman, aged fifty, was seized with sudden acute pain in the left knee. The next day the knee was swollen and painful on motion. During the following days the knee became more swollen and painful and the patient had a fever.

The patient was admitted to the hospital on the tenth day. The history showed no evidence of any previous infection. The temperature was 103°F., the pulse rate 100, and respiration 25. The blood pressure was 125/85. The left leg was swollen from the hip to the ankle and was easily twice the size of the right leg. This increase in size of the leg was due primarily to a pitting edema limited to the dependent aspect of the leg from the left hip to the ankle. Large engorged veins were present over the patellar and lateral aspects of the knee, and other signs of inflammation were present. There was effusion of the knee joint, the patella was ballotable, and the knee joint was very tender and hot to touch. Movement of the joint was painful and limited. Fluctuation was present. No lymphadenopathy was present in the left groin.

A diagnosis of acute septic arthritis was made. The first aspiration produced 310 cc. of thick yellowish-green pus from the knee joint, and examination revealed type XII pneumococci in pure culture.

Sulfadiazine was given in full dosage. The patient's temperature subsided on the fifth day and was only slightly elevated after that. A second aspiration produced 340 cc. of pus. Five grams of sodium sulfadiazine dissolved in 100 cc. of distilled water was then injected into the joint. Aspiration was repeated on the sixteenth, nineteenth, and twentieth days but no organisms were found in the pus.

X-ray films did not reveal any bone destruction in the knee joint. The hemoglobin averaged 58 per cent and the red count averaged 3,410,000; one transfusion was given. The high white-cell count was 12,200 and all other counts averaged 7,460. The differential counts did not show more than 76 per cent polymorphonuclear leucocytes. Six blood cultures failed to yield a growth.

The patient was discharged on the thirty-second day with a painless knee joint and was able to walk without discomfort. The range of motion was 90 degrees.

The listed cases of pneumococcic arthritis are given. The classification of the symptoms, clinical features, bacteriology, pathology, treatment, and prognosis are discussed in detail.

RICHARD J. BENNETT, JR., M.D.

Boger, W. P.: Purulent Meningococcal Arthritis. *Am. J. M. Sc.*, 1944, 208: 708.

Two proved cases of purulent meningococcal arthritis are presented, and it is suggested that the prognosis in joint manifestations of meningococcal infections is not so uniformly favorable as is usually stated in the literature.

Case 1. A fifty-two-year-old white widow entered the hospital with a temperature of 103° F. She complained of pain in "every joint." Several weeks previous to entry the patient had been complaining of vague, coldlike symptoms with general muscular aching and nausea. Physical examination after hospital admittance disclosed a fine purpuric rash over the ankles and lower thirds of both legs, and, in addition, several petechiae on the thighs and abdomen. Scattered over both hands, forearms, and feet were several larger purpuric spots which measured from 3 to 10 mm. in diameter. Resemblance was noted to erythema nodosum, and to Haverhill fever; the general picture exhibited redness and swelling of spots, redness and exquisite tenderness over both elbow joints, both ankle and wrist joints, and swelling of the hands and feet. There was a splotch of purple discoloration over each of the metacarpophalangeal joints and the dull red of inflammation about both wrists.

Aspiration of the left knee was done and approximately 50 cc. of thick, yellow pus was obtained. On smear, countless numbers of both intracellular and extracellular gram-negative diplococci were found. Later, both the blood culture and the culture made from the joint fluid were reported as showing growths of meningococci. The organism was typed as a type I meningococcus by the National Institute of Health.

After nineteen days of therapy with sulfadiazine the white count was 3,200, the patient was running a mild fever, and most of the joints had become painless, but the left knee was still swollen, and the right hand was still definitely swollen. The knee could be flexed beyond 90 degrees but it felt "stiff." Grasping with the right hand was poor and the wrist could not be dorsiflexed.

The follow-up of this patient revealed that on the eightieth day from the onset of her arthritis the left knee still ached, the left ankle swelled after walking, and the right hand remained swollen. A roentgenogram of the right wrist revealed "destruction and narrowing of the joint space due to infectious arthritis."

Case 2. A white, single woman, twenty-four years of age, had been employed in social work for several months and had been visiting in numerous homes.

She was taken with a "cold," headache, muscle soreness, and a rash. Examination revealed a temperature of 102° F., slight soreness of the muscles generally, mild headache, and some nausea. The neck was slightly painful on anterior flexion. The skin presented a hemorrhagic rash limited to the arms and legs, and both palms and soles presented spots ranging from 5 to 10 mm. in diameter. A lumbar puncture was done and slightly cloudy fluid was obtained; this revealed 500 cells per cubic millimeter. Organisms were not seen on smear, but culture of the fluid was positive for meningococci. A blood culture taken at this time was noted to be positive for meningococci. The left knee was somewhat swollen, but the patient herself had not been aware of this fact. There was no pain on manipulation of the joint, but flexion was a trifle limited by a feeling of "fullness." There was no redness or tenderness. Aspiration was done and a thick, yellowish fluid was obtained which, on smear, revealed gram-negative diplococci. Culture of this fluid was positive for meningococci. The patient recovered without later sequelae under treatment with sulfadiazine.

JOHN W. BRENNAN, M.D.

Shank, R. E., Gilder, H., and Hoagland, C. L.: Studies on Diseases of Muscle; Progressive Muscular Dystrophy; A Clinical Review of 40 Cases. *Arch. Neur. Psychiat.*, Chic., 1944, 52: 431.

A clinical study of 40 patients with progressive muscular dystrophy gave evidence of the hereditary nature of the disease. Fourteen of the 40 patients were from families in which other cases of the disease had occurred. There were examples of dominant sex-linked and simple recessive types of inheritance. Both pseudohypertrophy and atrophy existed in the affected muscles, with pseudohypertrophy most frequent in the large bulky muscles of the younger patients.

The early onset of the disease was demonstrated, the first symptoms having been noted by 62 per cent of this series of patients before the age of ten years. When the onset was delayed until late childhood or early adult life, the first muscles involved were frequently those of the scapulohumeral group.

The course of progressive muscular dystrophy was most rapid in patients with onset of the disease before the fifth year of life.

There were characteristic changes in the roentgenograms of patients with progressive muscular dystrophy. These alterations include conspicuous streaking of the soft-tissue shadows of affected muscle, delayed appearance of centers of ossification in the bones of the hands and in the epiphyses of the long bones, and demineralization of other bony structures.

The rate of excretion of creatine was greater, and the rate of excretion of creatinine was less in boys with muscular dystrophy than in normal boys of the same age group who were maintained on diets of identical composition. These differences were increased when the subjects were fasting.

The concentration of creatine in the plasma of dystrophic children was greater than the concentration in the plasma of normal subjects. Levels of creatinine in the plasma were unchanged.

The creatine tolerance of children with progressive muscular dystrophy was not significantly different from that of normal children of the same age group.

The basal metabolic rate was low in children with the disease. The median basal metabolic rate for a group of 14 patients was 14.5 per cent of the normal standards.

The fasting level of the blood sugar and the response to intravenous administration of dextrose were essentially the same in dystrophic patients as in normal subjects. One patient with muscular dystrophy gave evidence of an increased rate of utilization of dextrose injected intravenously.

Patients with progressive muscular dystrophy were in positive nitrogen and phosphorus balance.

Within recent years various types of therapy, including treatment with aminoacetic acid, vitamin E and pyridoxine, have been proposed for progressive muscular dystrophy. After thorough trial, each of these methods has proved to be singularly ineffective. Any rational approach to the successful treatment of the disease depends on more specific information concerning its nature and the metabolic changes affected by it.

ROBERT P. MONTGOMERY, M.D.

Grieve, J.: Congenital Subluxation of the Acromioclavicular Joint. *Lancet*, Lond., 1944, 247: 817.

Six cases of congenital subluxation of the acromioclavicular joint are described, also a seventh milder case with gross deformity of the right acromion. The exact nature of the condition is still obscure.

Even 1 cm. of displacement of the clavicle may produce no disability. The emotional effect may be important.

ROBERT P. MONTGOMERY, M.D.

Briede, P. C.: Tuberculosis of the Greater Trochanter and Its Bursa. *Radiology*, 1945, 44: 32.

The author gives a brief review of the literature which indicates that tuberculosis of the greater trochanter and its bursa is a rare condition usually occurring secondary to tuberculous osteomyelitis of the greater trochanter. All writers agree that complete extirpation of all infected tissue, with immobilization of the affected part, followed by body-building postoperative care, is the treatment of choice.

The condition may occur in either sex and at any age although it is unusual in children. The most common complaint is mild pain in the involved leg with intervals of quiescence. Often there is a draining sinus in the region of the trochanter.

Examination shows slight swelling with tenderness to pressure but no heat or redness. There is no limitation of motion in the hip joint. Tuberculosis elsewhere in the body is quite common.

The lesion has a strong tendency to recurrence and in the later stages it extends to the neck and head of

the femur and even to the joint itself. When only the bursa is involved, the percentage of cures is believed to be somewhat higher.

The first roentgen sign is a small fleck of calcium in the bursa or a minimal area of destruction in the outermost part of the trochanter which often can be demonstrated only with soft-tissue exposure. Later a larger area of destruction is noted in the trochanter, with osteoporosis of the adjacent bone. Sometimes an involucrum is found in the soft tissues lateral to the trochanter, secondary to infection or injury to the periosteum either following operation or in draining sinuses of long duration.

The differential diagnosis includes simple nonspecific bursitis or osteomyelitis and certain osteolytic neoplasms.

The author observed 4 cases which are briefly described and illustrated with the respective roentgenograms. T. LEUCUTIA, M.D.

Keen, P.: Pellegrini-Stieda Disease in the Bantu. *Clin. Proc.*, Capetown, 1944, 3: 331.

The author describes 17 cases of Pellegrini-Stieda disease in the Bantu. A total of 20 cases were observed in eighteen months.

The anatomy of the medial collateral ligament in the Bantu has been described and differences have been noted. It appears that the medial collateral ligament in the Bantu is a larger structure, the insertion of which into the condyle of the femur is intimately associated with that of the tendon of the adductor magnus. Its insertion into the tibia is similar to that of the hamstring muscles.

In addition, it was noted that there were cellular spaces around the tendon of the adductor magnus, particularly between this tendon and the vastus internus, where a branch of the geniculate artery passes forward. This space communicates with the upper insertion of the medial collateral ligament and could harbor a hematoma which might undergo ossification if osteoblasts were released by the trauma. This might explain the tendency of the ossified masses to extend upward beyond the limits of the medial collateral ligament.

In 10 of the 17 cases in this series, as judged from the roentgenological appearances, the ossification had extended beyond the limits of the ligament. In 4 other cases the ossification did not appear to be in the ligament at all, and in only 3 cases did it seem to be entirely confined to the ligament. For details on the etiology Kulowski's paper should be consulted.

In the present series of Bantu cases the intimate connection with the adductor-magnus tendon might account for the upward spread beyond the limits of the medial collateral tendons. This fact might also account for the frequency of this condition in the Bantu. The extra strain on the upper part of the medial collateral ligament where practically all the ossification occurs might be caused by the action of the adductor magnus which apparently has a direct connection with the medial collateral ligament in the Bantu. It is possible that the differences in anatomy might also account for the conspicuous absence of lesions of the internal semilunar cartilage in the Bantu.

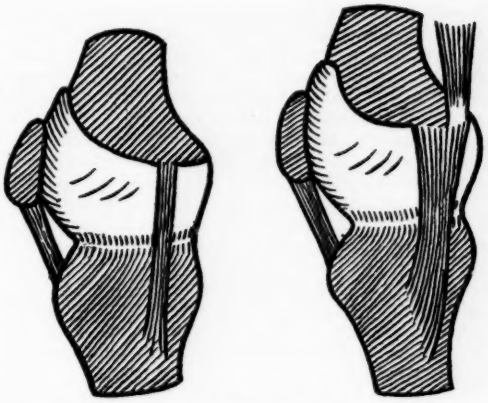


Fig. 1. Left, An average diagram.
Fig. 2. An average specimen in the Bantu.

It has been suggested that in the Bantu periosteal avulsion near the upper insertion of the medial collateral ligament is the commonest cause of this form of para-articular ossification.

The principle that the condition is a true post-traumatic lesion must be accepted on the evidence available.

In 1 case the first roentgenograph showed no abnormality, but the second one, taken twenty-three days later, showed definite signs of ossification. With a soft-ray technique the ossification would probably have been visible within eighteen days. Two other cases with negative roentgenographs at the time of the accident showed advanced roentgenological signs after ten weeks.

With the more extensive lesions in the Bantu permanent disability up to 20 per cent in certain cases may be expected. It should, however, be remembered that spontaneous resolution in mild cases may occur.

The temptation to dismiss a case of knee injury as trivial if no roentgenological signs are found must be avoided, particularly in view of the rarity of lesions of the semilunar cartilages in the Bantu.

The importance of this aspect of knee injuries cannot be too strongly emphasized.

ROBERT P. MONTGOMERY, M.D.

Simon, H. E., and Sacchet, H. A.: Muscle Hernias of the Leg. Review of the Literature and Report of 12 Cases. *Am. J. Surg.*, 1945, 67: 87.

The observation in 12 cases of muscle hernias of the leg form the basis of this report. Twelve case reports are given with a discussion of the etiology, symptoms and findings, the diagnosis, the differential diagnosis, the treatment, and the prognosis.

Muscle hernias of the leg are not of infrequent occurrence, particularly in active young males as represented by soldiers. Such hernias are characterized by a soft, semifluctuant swelling which increases in size when the limb is dependent or the muscle is related, and decreases in size or disappears when the leg is passively elevated and usually when the muscle involved is contracted. It is reducible on pressure, when a distinct fascial defect can be palpated.

There are three types: those due presumably to congenital defects; those due to direct trauma or to indirect muscle violence (usually single, large, and producing symptoms for which surgery is indicated); and the idiopathic type which appears spontaneously, particularly after muscular activity is increased. The last type is usually small, often multiple, presents less severe or no symptoms, and frequently requires no treatment.

Conditions to be differentiated from these muscle hernias are localized varicose veins, lipomas, angiomas, and other tumors. Surgical treatment consists of reduction of the herniated muscle and repair of the defect, usually by fascia transplant or suture.

EMIL C. ROBITSHEK, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Mowlem, R.: Cancellous Chip Bone Grafts; Report on 75 Cases. *Lancet*, Lond., 1944, 247: 746.

Seventy-five cases of cancellous chip grafting for the restoration of contour and of continuity in fractures of the facial and cranial bones, the mandible, and the tibia are reported. The results in all were successful, in spite of potential infection in some of them.

In all cases the graft is derived from the ilium. This bone is chosen for its relatively high cellular content and for its porosity. The fragmentation is designed to increase the surface area of the transplant and thus to create optimal conditions for survival of the greatest number of bone cells. The advantage of increased simplicity of the operative technique, although important, is secondary.

The ilium is exposed by an incision about 3 inches long, and its crest and outer plate are freed from their muscular and aponeurotic attachments. Occasionally this process is continued on to the inner aspect. A block of bone of sufficient bulk is then removed with an osteotome, and its cortical covering is discarded. The remaining cancellous mass is divided into chips of various sizes, usually about 1 by 0.5 by 0.2 cm. Irregular shapes are often useful, but it is undesirable to make the chips too small because excessive condensation is likely to occur.

The application of this principle may necessitate alternative methods of bone immobilization, but it simplifies operation and ensures much more rapid regeneration than the accepted methods of bone grafting.

The immediate survival of a bone graft probably depends on the establishment of a blood supply to its contained cells sufficiently early to ensure their continued activity.

For mechanical reasons, this is unlikely to occur in cortical bone but is much more likely to do so in cancellous bone.

Fragmentation of the cancellous bone renders a greater proportion of its cells accessible to the blood-supply and expedites its survival.

A considerable experience in the use of massive cancellous grafts from the ilium pointed to the probability that this type of bone survives from the beginning. The two most important facts underlying this belief are (1) the rapidity with which structural adaptation occurs, so that a new cortex is well marked on roentgenographic investigation in from eight to twelve weeks, and (2) the very high tolerance to infection which these grafts possess as compared with that of the more usual compact graft from the tibia.

GRAFTS FOR THE RESTORATION OF CONTOUR

The basic technique is always much the same. The graft depends for its survival on the blood supply and not on contact with existing bone. The correct contour is obtained by simply building up chips to the requisite levels. Fixation with a pressure bandage for from four to six days completes the procedure.

In all these cases operative technique has been much simplified, in that wide exposures, bevelling of cranial margins, accurate templates, tedious shaping of one-piece grafts, and difficult fixations have been eliminated. In their place is a restricted wound of access, and contour is regained by merely adding or subtracting the requisite number of bone chips.

GRAFTS FOR THE RESTORATION OF CONTINUITY

Thirty-six mandibular defects have been treated in which the loss has varied from ¼ inch to half the jaw, the average being 2 inches. The bone ends are immobilized by dental cap splints or external bone pins, or both. Eburnated bone and scarred soft tissue are widely removed. The first step in the insertion of the graft consists in placing a "distance piece" of cancellous bone, about ⅛ inch thick and ½ inch wide, into position on the deep aspect of the bone ends. This has a twofold function—it prevents soft tissues from bulging out through the mandibular defect, and it protects the chips from movement transmitted from the floor of the mouth. The chips are then laid into position overlying the distance piece and overlapping the mandibular ends, and are arranged to produce the necessary contour. No fixation other than suture of a layer of subcutaneous tissue is carried out, and it is sometimes desirable in the presence of free oozing to insert a drainage-tube for forty-eight hours. Three of these grafts were carried out in the presence of a known opening into the mouth, and many within a few days of the cessation of discharge. None were lost. The average time between operation and the removal of all splintage is 26.75 days, and it must be stressed that the chips

themselves confer no initial stability whatever. X-ray control shows that fusion begins to be visible between the chips and with the mandibular ends in about fourteen days, and continues until the bone is almost indistinguishable from the normal mandible. Clinical rigidity precedes complete roentgenographic fusion, so that careful examination and not x-rays is used to determine the point at which fixation can be discarded.

Five cases of extensive losses in the long bones, each associated with an overlying skin defect, have been treated on the same lines. Replacement of the skin defect has usually been the first step, although this may sometimes be combined with the bone-grafting operation. In the limbs treated to date, sufficient control of the bone ends was conferred by previously applied plaster casts, and a window was left, through which access was obtained, and this was closed at the end of the operation by a further application of plaster. This may not always be sufficient and actual skeletal fixation will then be needed. If this is so, either some form of skeletal splintage or a modified bony internal fixation may be used to confer stability. The chips can then be added to produce new bone.

It must be pointed out that the distance pieces are cancellous strips less than ⅛ inch thick, and that they in no way correspond with the usual type of inlay graft. They are simply "forms" between and around which the contour of the bone is built up with chips. They do not even fit snugly into their slots in the bone ends and they are neither wired nor tied in position. It will be seen that the bone ends themselves are not only cut back to eliminate eburnated tissue, but also bevelled to provide the maximal bleeding surface for adhesion to and vascularization of the grafts. It is unnecessary and undesirable to jeopardize the blood supply to the bone ends by stripping back of the periosteum through which nutrient vessels pass, and it is not justifiable to use power-driven saws or burrs because they may create sufficient heat to damage the vessels and the bone cells, on the immediate response of which the whole process depends.

In the tibial cases the initial plaster was removed at the end of five weeks and replaced by a below-the-knee walking plaster. This is done in an endeavor to ensure an early return to vascular normality in the limb. The time of removal of all splintage seems to vary with the length of the defect, with the degree of vascularity obtained in the bed, and with the stresses to which the graft will finally be subjected. A tibia with a 1-inch defect became rigid in ten weeks, while 2 other tibias with defects of more than 4 inches in length are still slightly springy at twelve weeks. In a personal communication, Plewes, who has applied this principal to a number of cases of nonunion of the tibia, radius, and ulna, without gross loss of bone, reports that all splintage has been discarded in a little less than seven weeks.

X-ray control in the tibial series here reported shows that the chips fuse with equal rapidity at the ends and in the middle of the defect, but that those chips lying immediately beneath the surface, where the blood supply is indifferent, do not fuse as fast as those in the depths of the wound which are in contact with vascular muscle bellies.

It will be appreciated, therefore, that in using cancellous chips the accepted standards of bone grafting are reversed. Instead of splinting the defect with a dense almost noncellular transplant which may also act as a bridge for osteogenesis or as a poor source of new bone—and for neither of these purposes is it histologically suitable—other methods of fixation are used and the defect is filled with a cellular mass, the survival of which will produce the requisite amount of new bone within a matter of weeks. The cases here reported appear to show that such a change of outlook is rewarded by increased operative simplicity, decreased postoperative recovery time, and added certainty of results.

ROBERT P. MONTGOMERY, M.D.

King, D.: Internal Fixation for Lumbosacral Fusion. *Am. J. Surg.*, 1944, 66: 357.

Recently the number of patients operated upon for the removal of displaced intervertebral-disc substance has increased tremendously and it has become apparent that some of these patients should

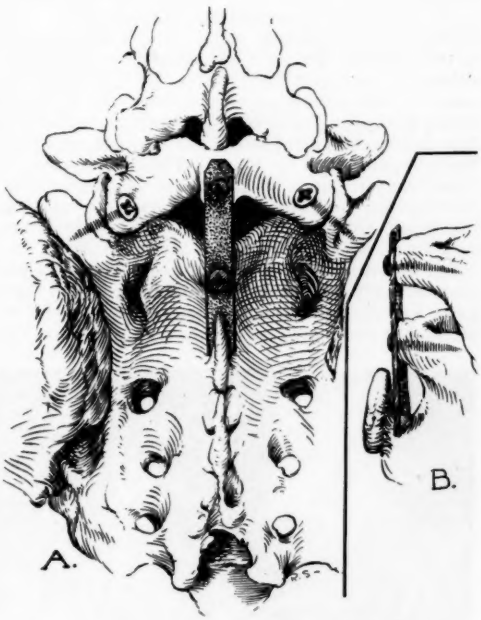


Fig. 1. A, Posterior view of lumbosacral joint showing screws through lateral articulations and tibial graft screwed to spinous processes. Multiple chip grafts are not shown. B, Lateral view showing tibial graft.

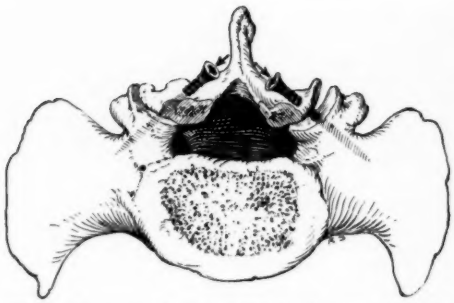


Fig. 2. Sacrum and arch of fifth lumbar vertebra (from above) illustrating direction of screws.

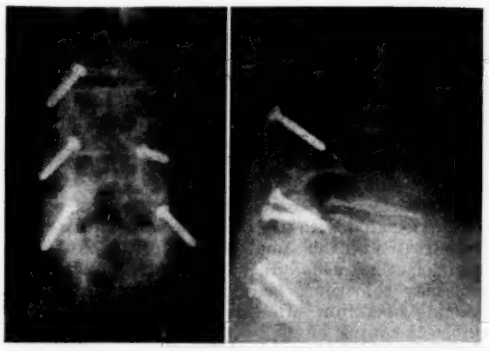


Fig. 3. Case 1. Roentgenograms taken fourteen months after operation. Right, Shows excellent posterior bony bridge.

be subjected to spinal fusion at the same time. Unfortunately, the prolonged bed rest in plaster has always been a serious objection to the operation and deterred many people from it. The purpose of this article is to describe an operative technique for fusing the lumbar and lumbosacral regions which furnishes immediate rigid internal fixation and thus eliminates the necessity for external fixation and prolonged bed rest.

The patient is placed prone on a hinged table and the lumbar lordosis is partly obliterated by lowering of both the head and foot ends of the table. The midline incision extends well down over the sacrum so that the muscles can be detached from the dorsal surface as far laterally as the posterior sacral foraminae. With a sharp elevator the muscles and ligaments are quickly and completely cleared from the fifth lumbar spinous process and laminae, and partially elevated from the fourth. The latter maneuver is necessary to get good exposure of the fifth process. Interspinous and supraspinous ligaments, and all other soft tissues are carefully removed from the area to be fused. The lateral articulations are exposed by dissecting and scraping away of their posterior capsular covers and slight opening of their joint spaces by strong traction with bone hooks under the laminae. As much as possible of the articular cartilages is removed and then a flat, thin, flexible cautery tip is inserted into the joint and the remaining cartilage cauterized. The fifth lumbar spinous process is removed and put aside for use as graft material at the close of the operation. The sharp edge of the small osteotome or a small gouge can be used to make a notch in the middle of the cortical surface of the inferior articular facet of the fifth lumbar vertebra for the reception of the tip of a No. 31 drill. This is necessary to prevent "wandering" of the drill point when it begins to rotate. If the drill is directed downward and outward parallel to the inferior edge of the fifth lamina (Fig. 1), the resulting tunnel will pass through the middle of the two facets that make up the joint and on into the lateral mass of the sacrum (Fig. 2). A vitallium screw* is placed in the tunnel and tightened, and the same procedure is carried out on the other side. Rigid lumbosacral fixation can be demonstrated by seizing the stump of the fifth lumbar spinous process with a heavy Kocher hemostat and lifting upward.

The remainder of the operation consists in elevating multiple small bone chips from the fifth laminae

*For women and small men ¾ inch long; for large men 1 inch long.

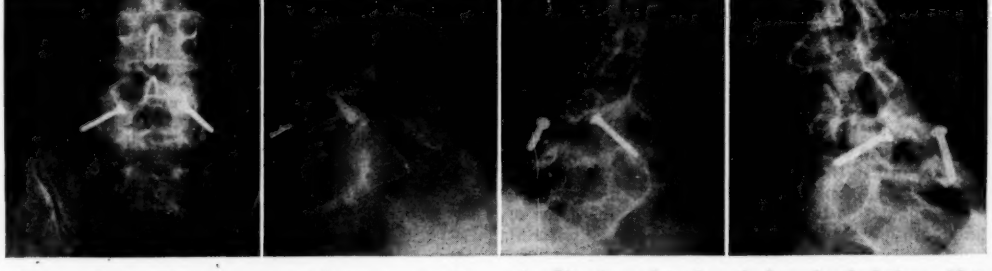


Fig. 4. Case 2. Roentgenograms taken one year after operation. a, Anteroposterior arrow marks site of laminectomy. First two films are left and right oblique views (60 degrees) to show the lateral articulations. Note complete disappearance of joint spaces. (Courtesy of American Journal of Surgery.)

and the dorsal surface of the sacrum. Supplemental bone grafts from the ilium or tibia are always used by the author, ilial bone being preferred. In an occasional case in which the spinous processes are well developed, a tibial graft has been fastened directly on top of the stumps (Fig. 1) with short vitallium screws. After closure several drain pads are snugly strapped over the wound with adhesive, but no brace or cast is used.

The patients are allowed to move about at will. Since internal fixation is rigid, the amount of pain is minimal. Many of the patients are up and about in ten days, but the average is about three weeks.

In 1 patient there was persistent burning pain in the distribution of the fifth lumbar nerve root on one side which necessitated the removal of the screw. In a series of 30 fusions the authors have had one postoperative infection. The screws and grafts were removed during the second postoperative week. Three case reports are presented.

ROBERT P. MONTGOMERY, M.D.

White, J. W., and Stubbins, S. G., Jr.: Growth Arrest for Equalizing Leg Lengths. *J. Am. M. Ass.*, 1944, 126: 1146.

The procedure presented in this report has been in use for ten years by the authors and has been found to be a simple and effective means of arresting the longitudinal growth of bones. In a series of 149 cases arrested before 1943 there were 202 separate growth arrests, the arresting of both bones below the knee being called one arrest procedure. Since that time more double arrests have been done, almost half the cases having had growth arrests both above and below the knee.

The operation employed in this series consists of the removal of a square core of bone and epiphyseal cartilage from the lateral and medial aspects of the distal or proximal end of the bone attacked with a slightly modified one-half-inch-square mortising chisel. The chisel is driven into the cancellous bone diagonally over the epiphyseal plate, a skin needle being used as a direction finder. The epiphyseal plate, if the operation is done correctly, should divide the excised square plug of bone diagonally in halves. After being driven sufficiently deep, the instrument is manipulated so that the square plug of bone breaks off in the depth of the hole, and the chisel containing the plug is extracted. The parts of the plate adjacent to the hole are thoroughly curetted, and the chisel, still containing the plug, is rotated 90 degrees from its original position and reinserted into the hole. With an obturator the plug of bone is driven out of the chisel into the hole. Thus the fragment of the epiphyseal plate in the plug of bone is rotated 90 degrees from its original position, which produces a deep bone graft bridging the cartilaginous gap. This procedure is carried out on either side of the femur or tibia, but the fibula needs to be attacked only from its lateral aspect. The joint is immobilized in plaster for a period of three weeks.

In order to record discrepancies in leg length more accurately than can be done with a tape measure, x-ray films of the patient's pelvis are made, with his feet forced firmly down against the foot board at the end of the Bucky table and a standard tube distance. The difference in height of the femoral heads from the transverse foot board is recorded as the difference in length of the legs. The same error is present in all the films and, as all calculations are based on these films, the error cancels itself. These films have proved to be valuable and accurate records.

A simple method of calculation, sufficiently accurate, in the face of so many variable factors associated with bone growth, is presented. Regardless of the age and size of the child, the authors calculate that a growth-arrest procedure at the distal femoral epiphysis will retard growth at the rate of 3/8 inch a year, while at the proximal end of the tibia and fibula it will retard growth 1/4 inch. They figure that growth ceases in boys at seventeen and in girls one year earlier. These figures have proved sufficiently accurate in a large number of cases. These methods of calculation and of keeping records, as well as the operative procedure, are recommended because of their effectiveness and simplicity.

JOHN L. LINDQUIST, M.D.

FRACTURES AND DISLOCATIONS

Siris, I. E.: External Pin Transfixion of Fractures; An Analysis of 80 Cases. *Ann. Surg.*, 1944, 120: 911.

The author reports the results of his experiences with the use of external pin fixation in the treatment of 80 cases of fractures during the past three and one-half years at the Bellevue Hospital in New York. He believes that the high incidence of discharge around the pin sites alone is sufficient reason to preclude the use of the method as a routine procedure. Many of the infections around the pin sites might have been averted by laying less stress on ambulation and mobilization of the joints, by immediate immobilization of the extremity and pins in plaster, and by the application of a new encasement when the swelling had subsided. The high mortality in hip fractures might have been prevented by the use of internal instead of external pin fixation. In the author's opinion, external pin fixation should not be used in the treatment of fractures of the hip. External mechanical fixation with plaster is useful if it is restricted to certain problem fractures in which conservative treatment will not give a satisfactory clinical result.

The author calls attention to the fundamental principles in the application of external pin fixation, which have evolved as a result of the use of this method by proponents, and as a result of his own experience. He describes the procedure of reduction for simple and compound fractures, the complications, the incidence of infection at pin sites and the time required for these sites to heal, the relation

of the healing time of the fracture to the time required for the pin sites to heal, the time required for the healing of fractures treated by external pin fixation, and the indications for the use of external pin fixation.

A number of illustrations and several tables accompany the article.

As a result of his experience with these 80 cases the author believes that the high incidence of discharge from the pin sites (46 per cent), of osteomyelitis of the pin sites with persistence of discharge long after the fracture had united (22.5 per cent), and of death (10 per cent) should preclude the further use of the method as a routine procedure for fractures of the long bones and of the neck of the femur. The procedure should be used only in selected cases, and by those who have been especially trained in the technique. The potential danger of infection at the sites of the pin insertions transcends the dangers of distraction, delayed union, and nonunion. The method should be restricted to certain problem fractures and to persistently displaced compound fractures in which, by visual manipulation, the reduction can be facilitated and maintained until a properly fitting encasement can be expected to maintain the realignment of the fragments. Ambulation and early mobilization of the joints should not be the motivating factors for the use of external mechanical pin fixation.

Infection of the pin sites with distraction and delayed union are attributed to (1) ambulation and motion of the joints without plaster; (2) function of the soft tissues against a pin which causes the infection and osteomyelitis; (3) pressure necrosis of the bone caused by a pin which impairs the stability of the fixation; this permits a continuous hyperemia of the fracture site with absorption of the ends of the bone, and results in distraction of the fragments; (4) the prolonged use of the pins; (5) failure to immobilize adequately the extremity and pins in plaster; and (6) failure to reapply a more snugly fitting encasement when the swelling subsides.

EMIL C. ROBITSHEK, M.D.

ORTHOPEDICS IN GENERAL

Perkins, J. E.: The Epidemiology of Poliomyelitis. *N. York State J. M.*, 1945, 45: 159.

The present knowledge of the spread of poliomyelitis is similar to what we knew about eighty years ago with regard to cholera and typhoid fever. At that time physicians concluded that cholera and typhoid fever were caused by drinking water polluted by the excreta of infected individuals. This theory proved to be a fact years later when the cholera and typhoid-fever organisms were discovered.

Poliomyelitis is caused by a filtrable virus. In the absence of a suitable laboratory animal considerable difficulties have been encountered in direct laboratory experimentation. Most of our knowledge of the spread of poliomyelitis depends entirely upon epidemiologic evidence. There are apparently several ways of spreading poliomyelitis. The usual manner of spreading poliomyelitis is discussed in this article. In order to understand the epidemiology of poliomyelitis it has to be borne in mind that only a small number of cases affected by poliomyelitis develop paralysis. In areas where poliomyelitis appeared in epidemic form the virus was found in the stools of many persons who had never shown any symptoms of paralysis. Another interesting observation in connection with susceptibility to poliomyelitis is the observation that in a community that had once been affected by this disease new cases of poliomyelitis are very rare. The same condition could be observed in the case of measles and other diseases with a high rate of infection and with a high degree of immunity resulting from the infection.

It has been accepted that the disease is spread by man himself. It is conceivable that the virus might be harbored by animals and insects under certain unusual circumstances. The actual portal of entry in poliomyelitis is the pharyngeal mucosa, and at times the lower intestinal tract. Faber, Silverberg, and Dong reported that in their experiments with cynomolgus monkeys, invasion of the central nervous system had been via the trigeminal nerves and via the sympathetic fibers of the nasopharynx. The peak of poliomyelitis usually occurs in the summer when also certain insects are prevalent. It must be stressed, however, that the prevalence of the infection in summer time does not exclude person-to-person spread of the disease. Although poliomyelitis is rarely seen in the cold season, the statement that poliomyelitis disappears as soon as there is a frost is not correct. Another factor in doubting that poliomyelitis is usually spread by insects is the fact that malaria, a disease known to be spread by insects, does not follow the clinical, laboratory, and epidemiological pattern of poliomyelitis. The poliomyelitis virus has been demonstrated on flies. These flies apparently come in contact with human excreta. The fact that the elimination of horse stables and privies in larger cities did not eliminate the disease indicates that flies have very little bearing on the spread of the disease. It has been clearly shown that water has no influence in the outbreaks of poliomyelitis in certain regions. In the years 1916 and 1925, it was found that raw milk was the means of transmission of poliomyelitis in only 7 or 8 cases. Since that time a considerable amount of evidence has been accumulated to show that milk is not usually involved in the transmission of poliomyelitis.

In considering the transmission of the disease through person-to-person contact, it was frequently possible to demonstrate the radial spread of poliomyelitis. This has been observed in many other respiratory-spread diseases, for example, measles. The fact that poliomyelitis is more frequently seen in rural communities might be explained by the fact that in larger communities the encounter with a poliomyelitis virus takes place at an early age. It is likely that for this reason there is a certain amount

of immunity against the disease. In smaller communities there is less contact between individuals, and the first encounter with this disease usually occurs at an older age.

In considering effective control measures, based upon the theory of person-to-person spread, rigid isolation of the affected individuals would be indicated. The effectiveness of this program is doubted when one considers that ordinarily only paralytic cases are reported to the Health Department. These cases, however, account for only a small portion of affected persons, and by the time the case is reported the patient usually has had ample opportunity to spread the disease. Parents living in the affected areas are advised to keep their children from gatherings and to avoid contact with children that show *any* signs of illness. Overfatigue, chilling, and tonsillectomy should be avoided in an area in which poliomyelitis is occurring. From a scientific point of view there might be some doubt as to the wisdom of postponing the first encounter with the virus for adulthood. Effective control of poliomyelitis would be accomplished through a safe vaccine. Unfortunately, the methods employed to kill the virus in the vaccine also destroy its antigenicity.

Investigators in Chicago have developed an effective vaccine against the homologous mouse-adapted Lansing strain. This vaccine was produced by a newly developed method of ultraviolet-light irradiation. Before accepting this vaccine overenthusiastically for human beings it must be tried on many more mice and many more monkeys and with many more strains of poliomyelitis. It is possible that in a few more years the problem of poliomyelitis may be solved by active immunization.

GEORGE I. REISS, M.D.

Rogers, L. S.: Practical Points in Plaster Technique; Two Years of Experience in Forward Surgery with a Royal Army Medical Corps (Mobile) Casualty-Clearing Station, 1941-1943. *Austral. N. Zealand J. Surg.*, 1944, 14: 75.

The surgeon in forward areas fulfils two main functions: (a) the saving of life from immediate and grave battle injuries, and (b) the treatment of many other wounds, chiefly injuries to muscles and compound fractures. The first function will occupy some 10 per cent of his time. The permanent relief of pain and the minimization of sepsis in an already infected wound stand out prominently among the objectives of surgery as practiced in a casualty-clearing station. The surgeon there needs few instruments and little academic knowledge, but above all he requires experience. With experience come many tricks of the trade which make his work easier and more effective. Complete immobilization may be regarded as the keynote of all. It banishes pain, relieves shock, lessens sepsis, and allows healing to begin while the patient is still far from a base hospital where more effective measures are possible. Complete immobilization is just as necessary for "fractures" or injuries of the muscles and skin as it is for those of bone.

Loose army plaster-of-Paris. This is the most useful of all. It is easy to carry in bulk, is of good quality, and is easy to make up into bandages of any width. It is slightly slower in setting than "Cellona," and is cheaper. Indeed, the best plasters were made from alternate bandages made with loose plaster-of-Paris and "Cellona."

A plaster must be strong to serve its purpose. Often on the arrival of a convoy, broken and, therefore, pain-producing plasters were observed. Lower-limb plaster cases usually break just about the ankle or just below the knee, and they should therefore, be made stronger in these locations. Greater strength in these locations is required in a plaster used for travelling than in one put on at a base hospital.

Slabs are always broken, and are therefore mentioned only to be dismissed.

Adequate length is another important feature. Many plasters are too short, and as a result do not fulfil their function. Many patients come with the toes unsupported and therefore are subject to pressure from the blankets. Plasters for the lower leg arrive with the plaster prolonged about 4 inches above the knee. This part usually softens and, the limb having shrunk a little, movement at the knee readily takes place. It is better, therefore, to carry these plasters higher—indeed, as a routine, up to the groin—in order to avoid a painful limb. Application from the groin to beyond the toes is advised.

Adequate padding is also important. Opinions on this subject differ markedly, and the author's casualty-clearing station has undergone a reversal in technique from the completely "skin-tight" closed plaster to a split, lightly padded cast. The artistry of the nonpadded cast has given way to the safety of the padded cast. They have, however, always used felt over the heel and the malleoli, particularly the heel, for it is of little avail to have the tibia and fibula united at the end of ten weeks if the slough over the heel has not yet separated. It is thought better thus to play for safety, for once the patient leaves the casualty-clearing station the delays may be of almost any length until the next hospital or medical area is reached. When wool is not available, "split Gamgee" has been used. It is not so good, but can be made to answer the purpose.

Finally, a plaster must be easily and painlessly removable. Such incidents as the swelling of a limb, a bony point becoming painful, or some similar misfortune may arise at any time and call for immediate removal of the plaster cast. Padding prevents unshaven hairs from sticking to the plaster, and the use of the "greased pig" makes splitting and, therefore, removal easy. The greased pig is a thick, round, rubber tourniquet liberally smeared with "vaseline" which is laid on the limb after the limb has been covered with wool. The plaster is now applied in the usual way over the tube, and when it has just set the tube is pulled out, an elevated tunnel thus being left down the whole length of the cast. This is cut open

at once, 2 inches being left intact at each end for the purpose of holding the ends of the plaster together. Should now an urgent removal of the plaster become necessary, it is a simple matter to cut the two ends. The splitting of the plaster allows of expansion of the limb to minor degrees, and thus makes the cast safer without the loss of any of its powers of immobilization.

Each patient in plaster should be kept at the station for two days if possible. The first day is for thorough drying and setting, and the second to make sure that the plaster is comfortable. Every complaint about pain in a limb in plaster should be listened to. Pain means that something is wrong, and when pain is present plasters should be reapplied until they are comfortable.

The chief causes of trouble in plasters for wounds of the hand and wrist are: the slabs are too thin and break at the wrist; they are not molded around the arm to grip it; they do not in certain cases extend beyond the finger tips to protect them against jarring; and circular plasters cause stiff fingers and often swelling beyond. To avoid these troubles, the wound is attended to in the usual manner and a wet, shrunk bandage is applied around the arm down to the hand. A thick, long, wide slab is made and applied over the volar surface of the arm from just distal to the elbow joint to well beyond the finger tips. It is molded around the arm and into the palm, with the hand slightly dorsiflexed. The piece projecting beyond the finger tips is then bent back dorsally and heaped up to form a small bar just distal to the finger tips. The rest is molded back to strengthen the wrist part. The rim thus formed distal to the finger tips prevents movement, and injury, and makes a comfortable support in which the fingers can move if this is desired. A cast of this type is extremely useful in all inflammatory infections of the hand, and is recommended for these; it can be modified to suit conditions. However, in the main it stops pain, limits infection, and allows early resolution.

PLASTERS FOR FRACTURES IN THE LOWER LIMB

To avoid the usual troubles a plaster cast is applied in the following manner:

The limb is held in abduction, extension, and slight flexion at the knee, with the foot in plantar flexion. Cotton wool in rolls is applied from the groin to the toes. Three pieces of felt are held ready, one for the heel and one for each malleolus. The greased tourniquet is laid lengthwise down the limb over the wool, the metal end being caught between the first two toes and the other end being left at the groin. The plaster is applied first at the thigh and a strong and adequate case is made. A pause is made after the knee is covered so that the plaster may set with the knee in slight flexion. The rest of the plaster is then applied to the toes, the heel traction being kept up and care being taken that the foot is in the neutral position. A slab is now made about 20 inches long, out of two 6-inch bandages. It is applied to the back of the calf and up to the toes, so that 6 inches overlap the toes on the dorsal aspect. The slab is bound to the cast up to the toe level, after which the 6-inch overlap is turned back to the plantar surface, the slab thus being doubled and a shelf being left projecting 1 inch beyond the toes. A small slab of "Cellona" about 10 inches long, made from 4-inch bandage, is laid across the end of the major slab. The ends of it are then brought down on each side of the foot. The plaster is finished with one 4-inch bandage. This plaster is an adequate one, the toe cap never breaking. The toes should be seen to be capable of full movement.

PLASTERS FOR LARGE WOUNDS OF THE THIGH AND FRACTURED FEMUR

From a casualty-clearing-station standpoint, the only type of immobilization which has stood the test of desert travel is the "Tobruk plaster." Immobilization is the only principle of importance as far as the casualty-clearing-station treatment of fractured femur is concerned. The Tobruk cast produces the best immobilization possible, and therefore extension is unnecessary in the author's opinion. Some still desire it and therefore it has been included in the technique.

The wound is attended to and dressed. A suitable Thomas splint is chosen and bent at the knee, and slings are made. For those who desire extension, the leg is shaved and strapping is applied from the mid-thigh to beyond the toes, padding being put between the strapping and the malleoli. The whole limb is padded with wool and a complete plaster is applied from just distal to the groin to the toes, the knee being included in a slightly flexed position, the toes with a good stout toe support, and the foot in a neutral position. A "greased pig" is used to allow of splitting. A felt pad is placed under the heel. The encased limb is now put into the Thomas splint. The ring is pushed well against the ischium and well into the adductor region. Care is taken that the bend in the Thomas splint corresponds to the flexion of the knee. Three shell dressings are now used. One is pushed between Scarpa's triangle and the ring, and the other two are placed between the outer aspect of the thigh and the ring. The ends of the extension strapping are now tied and fixed to the end of the Thomas splint by a cord. A Spanish windlass is inserted and twisted tight. The leg encased in a complete cast is now fixed immutably to the Thomas splint by three 4-inch "Cellona" bandages. One is placed at the ankle, one at the knee, and one at the ring, the shell dressings being just taken in so as to fix them. The "greased pig" is withdrawn and the cast is cut, the customary 2 inches being left at each end. A Sinclair's footpiece (the iron hoop) is now firmly fixed to the end of the Thomas splint by a plaster bandage. This does away with the stretcher bar and allows the patient to be nursed in bed and handled easily in air transport. It supports the splint and the limb perfectly when its foot is put between two folded blankets.

In the case of fractures of the femur, high in the shaft or at the neck, the author has used a technique similar to that described, but has prolonged the cast proximally, so that it follows the line of the groin to the iliac crest, thus grasping the trochanter. The ring of the Thomas splint in this case will not slip over the proximal end of the plaster, but rests on it. Any attempt, therefore, at extension is impossible. This method combined with the use of a stretcher bar, to anchor the distal end of the limb firmly, allows the patient to travel comfortably.

The points in favor of this method are:

1. There is no rotation of the limb inside the plaster, for the limb and foot are encased.
2. The foot cannot drop or twist, and the toes cannot become painful because all are supported; at the same time free toe movement is allowed.
3. The raw surfaces of the wound itself are given immediate support.
4. Practically no hip-joint movement can take place if the end of the spint is fixed.
5. The method is simple, quick, and always has been efficient in the author's experience.

PLASTERS FOR WOUNDS OF SHOULDER GIRDLE AND HUMERUS: THE THORACOBRACHIAL CAST

On the patient's arrival, an anesthetic is given, the wound is treated and dressed, and the limb is bandaged to the side of the chest wall with a strong flannel bandage, the arm being kept in flexion. Next morning the following preparations are made.

One hour before the patient is brought to the theater, morphine (¼ gr.) and scopolamine are given. A further dose of morphine is given intravenously. The patient's co-operation is sought by explanation as to the procedure. He is made to sit up in the stretcher and the bandage over the forearm put on the night before is cut off. The forearm is now bandaged with the wet bandage, and a good volar slab is applied to the heads of the metacarpal bones. This is allowed to set hard, being the permanent hand support. The patient is now made to sit on a stool. His feet are widely spaced to get a good base, with someone holding his hand firmly. The rest of the previous night's bandage is removed quickly, the whole arm being freed, and incidentally considerable pain is caused for the time being.

A large pad of felt is applied over the injured shoulder girdle, care being taken that it covers the spine of the scapula, the lateral aspect of the humerus, and the clavicle. Three shell dressings do equally well for this purpose. Over the olecranon a thick felt pad is applied and everything is bound on, two rolls of cotton wool being put in the gutter between the chest and the arm. The author uses two 6-inch bandages for this in a modified Velpeau technique. The arm is kept flexed with the elbow brought forward toward the midline. The forearm is kept free from the bandage and is kept held with a slight forward rotation to allow room to work between it and the chest wall.

The plaster is now applied, a triangle being made with the base extending from the base of the neck to the olecranon on the injured side, and with its apex under the opposite axilla. Slabs are used to strengthen this. One extends from the base of the neck to the olecranon and embraces it. The other extends from the vertebral groove, passes around and forward to wrap around the lower and outer third of the humerus.

The whole humerus is now completely encased, and all that remains is to fix the forearm by means of a plaster sling in a flexed position over the front of the chest. With a 6-inch bandage a start is made over the injured shoulder; a sweep is made downward over the flexed forearm, underneath it, and then up under the opposite axilla, and so on to the original starting point. Three bandages suffice for this purpose.

At this stage the patient is no longer in pain. In contrast to his former condition, one of considerable anxiety and pain, he can now get up and walk away if too much morphine has not been given to allow it.

The fixation of the humerus. Additional points of importance in the fixation of the humerus are the following:

The apex of the plaster under the opposite axilla should be made narrow and firm. The cast should be kept as high as possible, so that it does not chafe the abdominal wall when the patient is in the sitting position. There should be free movements of the fingers and support for the hands. The whole cast should fit snugly, and allow little or no movement between the body and the cast.

The application of a thoracobrachial cast is the most dramatic procedure a casualty-clearing station ever does for a conscious patient.

ROBERT P. MONTGOMERY, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Ficarra, B. J.: Mesenteric Vascular Occlusion. A Presentation of 15 Cases. *Am. J. Surg.*, 1944, 66: 168.

Since 1895, when Eliot reported the first successful resection of the small intestine for mesenteric thrombosis, each year adds several reports of cases on this subject. This disease has a comparatively low incidence. A study of the literature on mesenteric occlusion reveals that the number of cases cannot be tabulated exactly.

To date it appears that about 554 cases of this disease have been reported, in 32 of which resection was successful. At Kings County Hospital, Brooklyn, the author encountered 5 cases during his surgical service. Further investigation revealed that 10 cases, diagnosed at autopsy or at operation, had been recorded at Kings County Hospital from January, 1935 to December, 1943, which gave 15 new cases. Among these cases, 3 operative survivals are recorded. This brings the total number of successful resections to 35.

As a general statement, it may be stated that the predominating cause of mesenteric occlusion in younger patients is found to be heart disease or infection. In older patients degenerative or premalignant conditions appear to be important etiological agents.

Attempts have been made to outline a clinical syndrome which might serve as a basis for the early diagnosis of mesenteric occlusion. Some believe that venous mesenteric occlusion can be segregated clinically from the arterial type. As it is very difficult to diagnose mesenteric vascular occlusion preoperatively or before death, it can be appreciated how much more difficult it is to differentiate the venous from the arterial type.

The belief that cardiac disease, especially auricular fibrillation, is a prerequisite for superior mesenteric arterial occlusion is not held by the author on the basis of his experience.

No pathognomonic findings are known. The onset of an acute surgical condition of the abdomen in an elderly patient may suggest this disease. Shock is more pronounced than in most other abdominal conditions with the exception of pancreatitis. Pain is out of proportion to the physical findings. Physical findings are usually variable degrees of tenderness, rigidity, distention, and absence of peristalsis. A previous fallacy was the fact that cardiac irregularities and bloody stools were considered necessary in the clinical picture of this entity.

In this series, occlusion occurred more frequently in the superior mesenteric vessels than in the inferior mesenteric vessels. Conservative therapy in cases of mesenteric occlusion is ineffectual treatment. Surgical intervention with radical resection of the involved loops (beyond the areas of edema) is the only hope for cure.

The author's mortality rate was as high as that reported elsewhere. This mortality ranges from 60 to 90 per cent, and is due to shock and loss of blood. The author believes that the appalling mortality associated with this disease can be lowered only by improvement in diagnosis.

Treatment is of no avail in those cases in which occlusion of the superior mesenteric artery produces gangrene of the entire small intestine. Treatment is also ineffectual in cases in which the patient's general condition is so desperate (due to shock, heart disease, toxemia, or liver damage) that any operative procedure cannot be contemplated.

JOHN E. KIRKPATRICK, M.D.

Imler, A. E., Beaver, M. G., and Sheehan, W. C.: The Value of Venography in Varicose Veins. *Am. J. Roentg.*, 1944, 52: 514.

Venography is a valuable aid in the diagnosis and treatment of the following vascular diseases of the lower extremity: thrombophlebitis, pulmonary embolism, anteriovenous fistula, venospasm, and varicosities.

The authors in this report are concerned with the efficacy of venography in selected cases of varicose veins. Ten per cent of healthy adults suffer from superficial varicosities. Before obliterating the superficial veins, it is taken for granted that the deep veins are patent. The standard examinations (Perthes and bandage tests) for patency of the deep veins will prove adequate in the great majority of cases. However, in order to prevent the recurrence of varices, a careful consideration must be given to the existing conditions. Recurrent varices may be due to technical errors or deep venous obstruction and stasis. Superficial varicosities associated with deep venous obstruction are compensatory and their obliteration will be promptly followed by a recurrence. In such instances the clinical patency tests may be normal and as a result may be misleading.

As contrast medium, a 35 per cent solution of diodrast is used. All patients are tested for diodrast sensitivity. Although the technique is not described in this article, it has been thoroughly described in a previous article (Papper, E. M., and Imler, A. E. *Surgery*, 1944, 15: 402). Three cases are reported in detail.

It is the opinion of the authors that positive evidence in venographic studies will defer surgical interference that might result in a permanent aggravation of symptoms and a recurrence of varicosities. Venograms are indicated in those patients suffering from varicose veins with a history of thrombosis or thrombophlebitis, pain and fatigue on walking or standing, edema or symptoms of orthostatic collapse, or major vascular anomalies. MAURICE D. SACHS, M.D.

Shapiro, M. J.: The Preoperative Diagnosis of Patent Ductus Arteriosus. *J. Am. M. Ass.*, 1944, 126: 934.

The author notes that since it is now possible to cure a patent ductus arteriosus by surgery, it is of utmost importance that the correct diagnosis be made, lest patients be subjected unnecessarily to a major surgical procedure, or those with this lesion be denied the possibility of surgical cure. Two types of patency of the ductus may occur. The duct may remain open as part of a serious developmental defect and be the only means by which the circulation can be carried on in a heart seriously impaired by congenital defects. Such patients have evidence of congenital heart disease. In the type of case which is curable by surgery, the patent ductus is the only defect present, and the heart is otherwise normally developed. Strictly speaking, the uncomplicated isolated patency of the ductus is not a congenital lesion as it occurs after birth and has nothing to do with developmental defects of the heart. In the normal newborn infant, the ductus closes within a few minutes after the first breath is taken. Recent studies suggest that failure of closure in uncomplicated cases of patent ductus arteriosus may result from lack of oxygenation of the blood, possibly because of obstruction of the air passages in the newborn child.

The author discusses in detail the sex and age incidences, the clinical characteristics, and the electrocardiographic and x-ray findings in the 62 patients in whom a definite diagnosis of uncomplicated patent ductus arteriosus could be made. In 23 instances, there was an opportunity of checking the diagnosis. The diagnosis was correct in each instance.

The diagnostic criteria of patent ductus arteriosus may be summarized as follows: (1) machinery murmur; (2) thrill in pulmonary area; (3) enlarged pulmonary artery; (4) enlarged and pulsating pulmonary vessels; (5) enlarged heart; (6) increased pulse pressure; (7) stunting of growth; (8) absence of cyanosis and clubbing of fingers; (9) normal electrocardiogram; and (10) history of heart disease from early childhood.

In the differential diagnosis, several cardiac conditions may be confused with patent ductus arteriosus. One of the most important, especially in infants and young children, is the so-called venous hum in which there is also a continuous murmur heard over the base of the heart. It is usually not as loud as the characteristic machinery murmur. Occasionally, the diastolic murmur of aortic regurgitation will simulate the machinery murmur. In aortic regurgitation, however, there is invariably a pause between the systolic and diastolic murmurs. These murmurs are usually heard lower down along the left border of the sternum.

Patients with interauricular septal defects commonly exhibit x-ray changes which simulate the findings in patent ductus arteriosus. On fluoroscopy, the contour of the heart may suggest that found in patent ductus arteriosus; however, in most instances the heart is considerably larger and more rounded in patients with interauricular septal defects.

In conclusion, the author notes that the diagnosis of patent ductus arteriosus can be made without error. Patients should not be referred for surgical treatment unless they show the characteristic machinery murmur. The only exception to the rule is the occasional patient with a large patent ductus who may exhibit no murmurs. Patients with cyanosis and clubbing of the fingers do not have uncomplicated patent ductus, and they cannot be treated surgically. Pronounced electrocardiographic changes are not a part of the picture of simple patent ductus arteriosus. HERBERT F. THURSTON, M.D.

Bettman, R. B., and Tannenbaum, W.: Ligation of Patent Ductus Arteriosus in the Presence of an Apparent Bacterial Endocarditis; Report of a Case Apparently Cured. *Ann. Int. M.*, 1944, 21: 1035.

The authors report in detail a case in which ligation of a patent ductus arteriosus was done in the presence of an apparent bacterial endocarditis in a young woman eighteen years old. Two years after the operation, the girl is well, healthy, and to all appearances is living a normal life.

The feasibility of ligation of a patent ductus arteriosus was first demonstrated by Gross. The fact that such ligation in the presence of what appears to be a bacterial endocarditis may result in the cure of the disease was definitely established by Touroff and confirmed in several other reports. Inasmuch as medicine operates very much as law, on the basis of precedent, it will take an accumulation of statistics from many cases before the medical profession in general becomes cognizant of this new therapeutic procedure. Therefore, the authors state their purpose of publishing the results of ligation of a patent ductus in the presence of bacterial endocarditis as they observe them. HERBERT F. THURSTON, M.D.

Nixon, J. W.: Surgical Ligation of a Patent Ductus Arteriosus Associated with an Aneurysm of the Pulmonary Artery. *J. Thorac. Surg.*, 1944, 13: 513.

The author failed to find in the literature a report of successful surgical treatment of a case of an aneurysm of the pulmonary artery associated with a patent ductus arteriosus. This fact led him to report the following case:

A nineteen-year-old white female was admitted with the chief complaint of dyspnea on exertion and a diagnosis of a patent ductus arteriosus. The patient's past medical history was negative except for a humming and roaring in her chest which was present since early childhood and was more pronounced when she was lying down. She tired easily and when exercising would develop palpitation, dyspnea, and precordial pain. Physical examination was negative except for a thrill over the pericardial region and a to-and-fro machinery murmur transmitted to the left axilla and back.

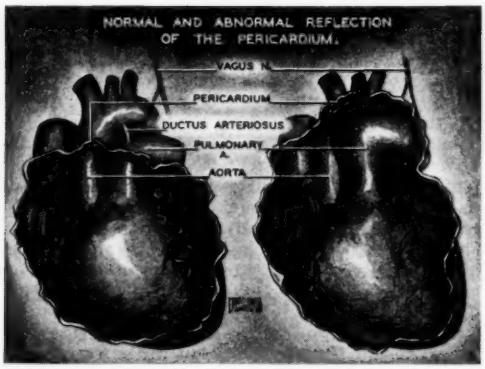


Fig. 1. Left, Position of pericardium as it is normally reflected from the pulmonary artery. Right, Pericardium reflected from the aorta as found in this case.

Laboratory findings were essentially normal. The patient was operated on under intratracheal cyclopropane anesthesia through the usual anterior incision over the left second intercostal space. When the pleural cavity was opened, an expansive pulsating mass was encountered within the pericardium extending upward in the region of the aorta. The pericardium, instead of being attached to the pulmonary artery as is usual, was attached to the inferior surface of the aorta and thus overlay the ductus (Fig. 1). On incision of the pericardium the mass was shown to be an aneurysm of the pulmonary artery, and only after the aneurysm was retracted downward could the ductus be exposed and dissected free. The ductus entered the aorta at a marked obtuse angle—a factor undoubtedly contributing to its patency. When the ductus was ligated with No. 8 braided silk, the thrill and murmur disappeared and the pulsation of the aneurysm markedly diminished, which indicated that the blood flow through the ductus under aortic pressure exerted an increased strain on the aneurysm wall. No attempt was made to deal with the aneurysm. The pericardium was closed with cotton sutures and the ribs with wire sutures. The patient had an uneventful rapid recovery with discharge on the eighth postoperative day. There was some laryngeal nerve injury due to the extensive dissection required to locate and free the ductus. The hoarse voice had disappeared by five weeks and the patient was working as a clerk with marked improvement in the dyspnea.

Although patent ductus arteriosus is next to patent foramen ovale as the most common congenital cardiac defect, aneurysm of the pulmonary artery associated with it is rare. Only 111 cases of aneurysm of the pulmonary artery were reported in the literature from 1833 to 1939 and a patent ductus was present in 23 per cent of these cases. The pulmonary hypertension associated with patent ductus has been regarded as a cause of pulmonary aneurysm, but since patency of this passage is common without aneurysm, it seems reasonable to assume that some additional lesion must contribute to its production. Syphilis has been considered also as an important causative agent.

Dilatation and thinning of the pulmonary artery may be present in cases of patent ductus arteriosus, but a true aneurysm is rare. This amount of thinning seems to depend on the diameter of the ductus and the completeness of its patency.

The failure of a ductus to close at birth is probably due to its position and direction. It usually enters the aorta at a right angle but as the acuteness of the angle decreases it becomes more exposed to intra-aortic pressure. If the angle becomes obtuse, the patency is maintained and a greater pressure and volume of the aortic blood passes into the pulmonary artery, the wall of which, not intended for such pressure, may yield to form an aneurysm. The presence of these two associated lesions leads to diagnostic confusion and adds another argument in favor of surgical closure of the recognized patent ductus.

ROBERT BIGELOW, M.D.

Alexander, J., and Byron, F. X.: Aortectomy for Thoracic Aneurysm. *J. Am. M. Ass.*, 1944, 126: 1139.

The authors successfully removed an aneurysm of the thoracic aorta measuring 11 by 8 cm., together with a 7.5 cm. length of the aorta. This is believed to be the first case of successful removal of an aneurysm of the thoracic or abdominal aorta or of successful ligation of the thoracic aorta. The patient was a white youth, aged nineteen, whose symptoms and physical signs led to a provisional diagnosis of aortic coarctation on the basis of extrinsic pressure by a neoplasm (Fig. 1).

Thoracotomy was performed under intratracheal ether anesthesia and a saccular aneurysm of the upper descending aorta was exposed in the costovertebral gutter. The upper pole was 5 cm. inferior to the left subclavian artery and the attachment to the aorta was about 7.5 cm. long. The pulsations in the aorta above it were strong but those in the aorta below it were only questionably palpable. The aorta at its junction with the upper end of the aneurysm appeared to be slightly constricted. The subclavian, internal mammary, and upper intercostal arteries were greatly enlarged. As the thin-walled aneurysm was in danger of rupture at any time and as the collateral circulation appeared to be adequate, resection of the aneurysm was decided on. The aorta just below the origin of the left subclavian artery was ligated with a 1.3 cm. wide cotton tape, and a silk ligature was placed between the tape and the place where the aorta was to be divided; the aorta was similarly ligated 4 cm. below the aneurysm. Three pairs of greatly enlarged intercostal arteries emerging from the aneurysmal sac were ligated and the entire aneurysm-bearing segment of the aorta was removed. The divided ends of the aorta were oversewed with silk, and a pedicled flap

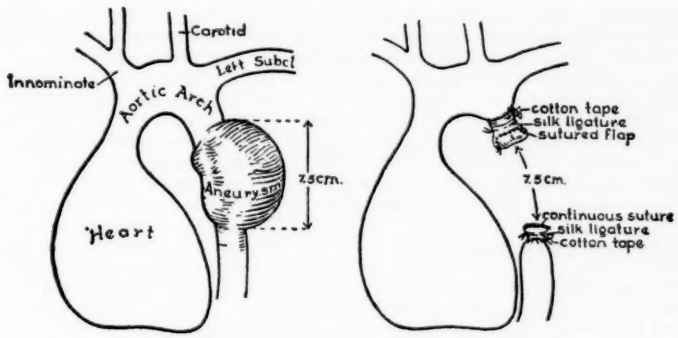


Fig. 1. Before and after resection of the aneurysm. Actually, the aneurysm was 11 cm. long; its attachment to the aorta was 7.5 cm. long.

of the posterior aneurysm wall was turned over the open end of the superior segment of the divided aorta and tacked to the aortic wall (Fig. 1).

The feet remained warm throughout the operation and afterward but there was a postoperative rise in blood pressure in the upper extremities. Acute cardiac decompensation occurred seventeen days after operation and receded rapidly under treatment. Up to three months after operation kidney-function tests were consistently normal but there was persistent hypertension with retinal angiospasm, exudates, and hemorrhages. One year after operation the patient's activities were the same as before operation, and examination showed the acute process in the retinas to be at a standstill although the hypertension was still present. Because of the persistent hypertension and angiospasm the prognosis of the condition must be guarded.

This aneurysm probably arose in connection with an aortic coarctation, the presence of which is presumed because of hypertension, a well developed collateral circulation, notching of the ribs, and the absence of pulsation of the aneurysm and of the aorta below it. This patient was unique in that all the factors essential to the success of the operation were present: his youth and good general health, the absence of syphilitic disease of the aorta, the presence of a well established collateral circulation, and the location of the aneurysm, which permitted the placing of the proximal ligature on the aorta below the left subclavian artery.

JOHN L. LINDQUIST, M.D.

Scott, V.: Abdominal Aneurysms. *Am. J. Syph.* 1944, 28: 682.

In a series of 96 cases of abdominal aneurysm of the aorta or its main branches, 58.3 per cent were syphilitic, 20 per cent arteriosclerotic, and 18.8 per cent mycotic. In 43 of these cases the aneurysm involved a branch of the aorta. Of the latter cases, 35 per cent were syphilitic and 18.6 per cent were arteriosclerotic, and in 41.9 per cent the aneurysm was caused by bacterial agents. Multiple abdominal aneurysms were present in 18.7 per cent of this series, and in 30 per cent arteriosclerosis was the causative agent. Aneurysms of the upper abdominal aorta, including those involving the celiac axis and superior mesenteric artery, were most frequently syphilitic, while those of the lower abdominal aorta were either arteriosclerotic or bacterial. Arteriosclerotic aneurysms usually occurred in patients over fifty years of age and of the white race; they were predominantly males. Luetic aneurysms occurred mainly in the colored race.

The symptomatology of abdominal aneurysm is dependent upon its size and location. Pain, especially of the nocturnal type, was characteristic in the luetic group. Often it was associated with vertebral erosion. Arteriosclerotic aneurysms were asymptomatic in 80 per cent of the patients. In the mycotic type, bacterial infection masked any aneurysmal symptoms. The presence of a pulsating expansile mass with palpable thrill and audible bruit was dependent on the size and location of the aneurysm. In 75 per cent of the luetic group, the latter physical signs were detected. In a differential examination it must be remembered that neoplastic or inflammatory tumors close to large arteries may give similar findings. Furthermore, intraluminal clotting may cause the thrill and bruit to disappear. The largest sized aneurysms were usually luetic, but in all groups the saccular variety predominated. Rupture of the aneurysm occurred frequently in from 39 to 41 per cent of the mycotic and luetic types—and hemorrhage extended commonly through the retroperitoneal tissues and less frequently into the peritoneal cavity.

Thirty-four per cent of the patients with luetic abdominal aneurysms also gave signs of aneurysmal involvement of the thoracic aorta. Erosion of the vertebra was common in the luetic aneurysms of the upper abdominal aorta. This was usually demonstrated by x-ray examination, which also revealed calcium deposits in the vessel walls.

The prognosis of syphilitic abdominal aneurysm was found to be variable but poor. In 70 per cent of the patients death ensued within thirty-six months after the onset of symptoms, and only 17 per cent lived more than five years.

As regards treatment, there has been little tendency to treat such lesions. However, Blakemore and Lord have recently offered a promising method of controlled electrothermic coagulation for aneurysms.

BENJAMIN G. P. SHAFIROFF, M.D.

BLOOD; TRANSFUSION

Invernizzi, D., and Yannicelli, S.: Distribution of the Rh Factor in the Population of Montevideo (Distribucion del factor Rh en la poblacion de Montevideo). *Arch. urug. med.*, 1944, 25: 185.

This article describes the first attempt at determining the frequency of the Rh factor in the blood of the population of Montevideo. The majority of the individuals examined were voluntary donors of blood in the Center for Blood and Plasma. Some determinations were made in the Maternity Hospital with the object of studying a case of fetal erythroblastosis which will be published elsewhere.

The anti-Rh sera used were from two sources. The first was obtained from a woman who gave birth to a child which died of fetal erythroblastosis. This serum contained an irregular agglutinin which was identified as anti-Rh. The other was a human anti-Rh serum given by the Rockefeller Foundation of New York.

The technique of the reaction is described. Among the 112 determinations, 92, or 82.14 per cent, were Rh-positive and 20, or 17.85 per cent, were Rh-negative. AUDREY G. MORGAN, M.D.

Macklin, M. T.: The Diagnosis of Rh Incompatibility, Especially by Microscopic Appearances; Its Relation to the Syndrome Formerly Diagnosed as Erythroblastosis. *J. Pediat.*, S. Louis, 1944, 25: 533.

Erythroblastosis as originally defined indicates the presence of large numbers of nucleated red blood cells in fetal livers at a stage in development when erythropoiesis should largely be absent from the liver. This is evidenced by the presence in the circulating blood of the fetus or newborn infant, of immature red cells, the type or quantity of which is not normal for that stage of development. Rh incompatibility is suggested as the term for the disease entity caused by a reaction between Rh antigens in the fetus and the specific antibodies in the maternal blood to combat them. This results in erythroblastosis due to hemolysis; but many conditions other than those involving incompatible Rh factors in mother and fetus are factors in the production of erythroblastosis. The author outlines diagnostic criteria of Rh incompatibility. Many of the criteria said to be diagnostic of Rh incompatibility may be found in other conditions and may not always be found in Rh incompatibility.

In order to diagnose whether a fetus is suffering from Rh incompatibility, it must be shown either (1) that the fetus possessed in its circulation antibodies against its own Rh positive cells, or (2) that the blood of the fetus and mother were of different Rh groups and that the fetal tissues showed departures from normal which were characteristic of the antigen-antibody reaction.

Probable Rh incompatibility can be diagnosed in the living infant when different Rh factors are demonstrable in mother and fetus, and an anemia, or jaundice, or both, unexplained by other conditions are present in the infant. The diagnosis is strengthened if other infants in the same family have suffered from fetal jaundice or from proved Rh incompatibility.

Probable Rh incompatibility can be diagnosed in the stillborn infant or in the infant after death when different Rh factors are present in mother and fetus, and when the fetal liver shows that hemolysis has taken place as evidenced by the presence of iron in the liver. This is determined by the Prussian blue technique.

Some of the criteria used for the diagnosis of Rh incompatibility are of value only when the fetus is full term, or when the infant lives for several days. They are not of value on fetuses lost early in pregnancy. The iron test is of value in these early cases.

Iron is not normally stored in fetal livers in such form that it is demonstrable by the Prussian blue technique; therefore, iron as revealed by this test indicates excess blood destruction. One of the most frequent causes of such excess destruction is Rh incompatibility. ERNEST E. ARNHEIM, M.D.

Camponovo, L. E.: The Study of Oxalic Acid as a Hemostatic (Contribucion al estudio del acido oxalico como hemostatico). *Rev. As. méd. argent.*, 1944, 58: 918.

The author reviews the work previously done on the use of oxalic acid as a hemostatic. Some investigators hold that it does act as a hemostatic, while others deny this property.

He reviews the physical properties of the acid, and its metabolism and pharmacology before he takes up the description of his experiments. A certain amount of this acid is found normally in the blood. The author gave it to dogs by intravenous injection in doses of 5, 10, and 20 mgm. The determinations of the coagulation time were made by the method of Lee and White. A control animal did not show any change in coagulation time in the various tests. Tests made ten minutes after the injection of oxalic acid showed lengthening of the coagulation time in some of the experiments, no change in some, and moderate shortening in others. The details of the results are given. Tests made twenty minutes or later after the injection showed shortening of the coagulation time, with the maximum shortening between fifty and seventy minutes after injection.

Oxalic acid was used clinically in 10 cases of hemorrhage in human subjects due to various causes.

The injections in these cases were made intramuscularly. The drug proved effective as a hemostatic, the maximum shortening of the coagulation time occurring one hour after the injection.

The exact manner in which oxalic acid acts in shortening the coagulation time is not known. Schumann suggests that it acts as a catalyzer, which assists the action of the calcium, platelets, and tissue fluids in forming thrombin. Page, Russell, and Rosenthal think that it changes the surface tension of the membrane of the platelets, and brings about the liberation of thromboplastic material in this way.

AUDREY G. MORGAN, M.D.

Beyer, K. H., Flippin, H., Verwey, W. F., and Woodward, R.: The Effect of Para-Aminohippuric Acid on the Plasma Concentration of Penicillin in Man. *J. Am. M. Ass.*, 1944, 126: 1007.

The authors note that when sodium para-aminohippurate and penicillin are administered simultaneously, the former compound competes with penicillin for the same renal tubular excretory mechanism. By doing so the rate of renal elimination of penicillin is much reduced, which slows up considerably the rate of fall of the plasma concentration of the antibiotic agent. A combination of these agents was administered continuously to experimental animals without the production of the functional or histomorphological changes attributable to the two agents. Moreover, it was shown that the acute toxicity of sodium para-aminohippurate was very low.

In view of the implications of the possible therapeutic efficacy of the combination, it was decided to obtain data on a few patients to determine whether the simultaneous administration of para-aminohippuric acid with penicillin produced an elevated plasma concentration of the antibiotic agent. A careful study of the patients for any untoward reactions was thereby permitted. The methods followed in the administration of penicillin to 9 patients are presented. The methods for the plasma assays of penicillin and of para-aminohippuric acid also are presented.

The results of the tests on these 9 patients are summarized in a tabulation. Examination of the table reveals that in every instance the administration of para-aminohippuric acid with penicillin caused at least a twofold increase in plasma concentration of the antibiotic agent. There was a definite relationship between the plasma concentration of para-aminohippuric acid within this range and the amount to which the penicillin level was elevated. There was no outstanding difference in response due to age, sex, or race.

The pharmacodynamic effects of sodium para-aminohippurate are considered in two categories: (1) those attending the injection of the priming doses, and (2) those occurring during or following the para-aminohippuric acid infusions. Only when para-aminohippuric acid was administered at room temperature was any reaction noted. The only noteworthy untoward effect which occurred following the administration of certain of the priming doses of para-aminohippuric acid was a contraction of the smooth musculature of the large intestine and bladder, unattended by pain or discomfort. The infusion of para-aminohippuric acid and penicillin continuously for twelve hours produced no discernible deleterious effects on the patients who manifested a number of unrelated disease entities.

The authors suggest that the plasma concentration of para-aminohippuric acid be checked frequently to make sure that the function of diseased kidneys is sufficient to allow excretion of the drug rapidly enough to prevent an excessive blood level of para-aminohippuric acid. Moreover, the authors note that more effective plasma concentrations of penicillin were found to be present in patients who had known renal involvement. In the light of recent work, this can be interpreted as being due to renal damage which decreases the transport capacity of the tubular excretory mechanism.

HERBERT F. THURSTON, M.D.

Opazo, V.: Retinal Hemorrhage following Transfusion (Hemorragia retiniana post-transfusional). *Bol. Soc. chilena obst. gin.*, 1944, 9: 153.

Attention was first called to the complication of retinal hemorrhage following blood transfusion by Sallmann in 1925. Since then a number of cases of retinal hemorrhage and one of permanent and one of temporary blindness following transfusion have been reported.

The author reports a case in a woman of forty-nine who was to be operated on for ovarian cyst after previous treatment to improve her general condition. The circulatory system was normal. She was given three blood transfusions, and about three and one-half hours after the third transfusion retinal hemorrhage developed.

After a discussion of the cases reported the author concludes that this complication occurs only when there are predisposing causes, such as long-continued anemia, and that it occurs most frequently when repeated transfusions have been given. He believes it is not a serious complication, although some students of the subject think it is.

AUDREY G. MORGAN, M.D.

Koop, C. E.: The Use of a Specially Prepared Gelatin Solution as a Plasma Substitute. *Surg. Clin. N. America*, 1944, 24: 1300.

Koop holds that gelatin is the best of the plasma substitutes and that it is equal to plasma in the treatment of shock. It is remarkably nontoxic and nonantigenic. The gelatin solutions used were specially prepared from selected raw materials to the finished product in a plant designed especially to prepare gelatin for intravenous administration to patients. Colloidal solutions such as gelatin are offered not as substitutes for whole blood but rather as substitutes for plasma. Plasma is used chiefly for its coagulating function, its nutritional value, its aid in the defense against infection, and for the proper-

ties associated with the colloidal osmotic pressure of its proteins. Whole blood is used more extensively than plasma for its antihemorrhagic and antibacterial properties. The chief use for which plasma is employed is for the colloidal osmotic pressure of the plasma proteins when the desired result is maintenance of an adequate blood volume and its many related physiological phenomena. It is for this particular purpose that gelatin solutions are used so efficiently.

The criteria for an ideal plasma substitute are the following:

1. Physical properties. An ideal plasma substitute should be stable, of low viscosity, and have a high colloidal osmotic pressure; and the colloidal particle size should be sufficiently large to cause it to be retained in the circulation long enough to be effective. Finally, there should be no difficult problems with storage.

2. Physiological properties. It must be safe for injection in large quantities, and it should not interfere with blood coagulation, the defense against infection, or tissue repair. It must be nontoxic.

3. Immunological properties. It should not be an antigen and it should have no natural sensitivity to similar substances such as foods or sera.

The gelatin solution which has been most satisfactory is one prepared by hydrolysis of alkali-treated long-bone collagen under controlled and standardized conditions. It is administered as a 6 per cent solution in physiological saline solution after autoclaving for twenty minutes. (This is the solution Knox P-20 referred to by the National Research Council in its report on Gelatin as a Plasma Substitute. J. Am. M. Ass., 1944, 125: 284.) This solution is preferred for the treatment of shock because its method of preparation produces the optimum molecular size of the gelatin, upon which its physiological action largely depends.

When gelatin solutions are subjected to high temperatures, such as those required in sterilization by autoclave, the long gelatin aggregate molecule is broken down to form a larger number of smaller molecular particles. Whereas the smaller molecules theoretically exert a higher oncotic pressure, they are excreted from the blood stream through the kidneys so rapidly that their effective oncotic pressure is short-lived and not of the sustained value of the larger molecules which actually exert a lower osmotic pressure. For this reason two factors are of importance in the manufacture of gelatin solutions for plasma substitute: the source of the gelatin and the method of preparation of the solutions. Bovine long bones are a better source of gelatin than skins, hides, or fish products because of their relative freedom from bacterial and fungus contamination and their uniformity of composition. Gelatin solutions for intravenous use should be prepared for that purpose and apart from the commercial manufacture of edible gelatin. Even the use of pure U.S.P. edible gelatin in the preparation of intravenous solutions may result in a pyrogenic product because of impurities that may render it unfit for parenteral use. There are several advantages in the preparation or processing of gelatin solutions. Whereas the preparation of plasma must be undertaken with the most rigid sterile technique, gelatin solutions, if prepared with reasonable cleanliness, can be thoroughly sterilized in the last step of manufacture by autoclaving and Seitz filtration. Gelatin solutions need not be refrigerated as fresh plasma must be, and they can be kept in a single container as compared with the two needed for lyophilized plasma. When the solution is prepared as a single dose package, no preservative need be added. This avoids the possible danger of chemical phlebitis due to preservatives. The great advantage of gelatin is that it is readily available at relatively low cost and that we are not dependent upon blood donations to obtain it. This is of special practical importance in localities and hospitals where plasma banks are not established.

Gelatin solutions are miscible with all of the usual intravenous solutions and can be administered by means of any of the "open" or "closed" methods. The open system, which is frequently used for transfusions of whole blood or plasma, has been satisfactory for use with gelatin. Unless heated, gelatin solutions of the type recommended are in the physical state of a gel at ordinary room temperature in the temperate zone. However, because the gelation point is lower than the melting point, these solutions, once warmed, remain fluid at room temperature unless exposed to a cold atmosphere such as that from an open window. Gelatin solutions kept in a warm closet at 37°C. are ready for immediate use. Inasmuch as there is a very slow deterioration, or shortening, of aggregate molecular chains, such solutions should not be stored at 37°C. over a month. An alternate method of preparation is immersion of the gelatin bottle in a hot water bath until melting takes place. Minimal viscosity and hence greater speed of infusion is found at 50°C. The return to the gel state does not occur until ample time has passed for administration at ordinary room temperature. As with plasma or whole blood, it is advisable not to use needles of a size smaller than 19 gauge for gelatin infusions. In the treatment of shock during which it is occasionally of advantage to administer gelatin relatively rapidly, an 18-gauge needle should be used. It has not been necessary in the cases treated to infuse gelatin under pressure, although there is no reason why such a method would be impractical because of any properties of gelatin. It is possible to administer a suspension of erythrocytes with gelatin. This is an inexpensive procedure in those places where erythrocyte suspensions are available without cost as a by-product in the preparation of plasma. One difficulty arises in the administration of gelatin-erythrocyte suspensions. Gelatin increases the sedimentation rate of erythrocytes, and thereby occasionally causes the needle to become plugged by the high concentration of cells in the dependent portion of the apparatus if some precaution is not taken. The addition of a 5

per cent dextrose solution in equal quantity facilitates the administration of gelatin and erythrocytes. A more complicated but certain method is to bubble oxygen through the mixture to keep the cells in uniform suspension. The size and frequency of infusion must be governed by the requirements of any given case. Gelatin infusions must be given with the same care as an infusion of plasma and may be given for similar indications.

The administration of single and repeated infusions of ossein gelatin has been accompanied by few local or general reactions. Venous thrombosis has occurred in less than 3 per cent of infusions. This was true even when phenyl mercuric borate was added to the gelatin as a preservative. No unusual difficulty has been encountered in local extravasations of gelatin solution from its accidental introduction subcutaneously. The use of hot wet dressings is of advantage in hastening the absorption of such collections.

THE CLINICAL USE OF GELATIN SOLUTIONS

Treatment of shock. Experience in treating shock following burns, hemorrhage, and trauma has demonstrated gelatin solutions to be effective. It is difficult in clinical practice to judge the comparative efficacy of a plasma substitute, as one is separated from the controlled conditions of the laboratory. Studies on volunteers bled into shocklike states while under observation on the ballistocardiograph have established the efficacy of gelatin in the treatment of hemorrhage on physiological grounds. As a routine in the treatment of shock an intravenous infusion of 6 per cent gelatin is started as soon as possible. Usually 500 cc. are sufficient to bring about a rise in blood pressure and pulse volume but occasionally more are required. It may be desirable to give another gelatin infusion several hours later or to give a whole blood transfusion. The rate of infusion is important in some cases of shock. It is customary to administer the solution as rapidly as it will flow by gravity through an 18 or 19 gauge needle. In cases of hidden hemorrhage an effort should be made to keep the patient out of shock but to maintain his blood pressure at a sufficiently low level, usually about 100 mm. of mercury systolic, to favor clot formation and to discourage brisk bleeding. One possible danger of administering large quantities of gelatin to such patients is that they may continue to bleed internally, but fail to show a fall in blood pressure or an elevation in pulse because of the maintenance of blood volume. The severe anemia which may develop is detected only by the observation of pallor or a marked fall in hemoglobin or hematrocrit reading.

Treatment of burns. Gelatin has been used to some extent in the treatment of burns, but E. I. Evans has treated a comparatively large series of second-degree burns with gelatin with success comparable to that obtained with plasma. He believes that repeated infusions of 500 cc. of gelatin solution every four to six hours is a better practice than less frequent larger infusions, and that after thirty-six or forty-eight hours, whole blood is usually indicated. Because of the size and shape of the gelatin molecule, it is likely that it is lost less readily from the surface of a burn than is plasma, although no accurate data are available. The probability of this phenomenon serves as a reminder, however, that while the blood volume and hematocrit reading might be maintained, the plasma protein can leak out of the denuded area to produce a severe depletion of natural serum proteins. With our present knowledge it would seem advisable to give whole blood or plasma to the patient treated with gelatin who survives the shock phase of his burn. The use of gelatin solutions intravenously in no way alters the use of adequate local treatment to the burned area.

As a supportive measure in operative surgery. In a patient about to undergo surgery under serial spinal anesthesia, a gelatin infusion before or during the procedure has very frequently prevented the expected fall in blood pressure. Especially in emergency surgery, under any type of anesthesia, the use of gelatin infusion during an operation has aided many patients in coming through an otherwise difficult procedure without the added danger of an unstable pulse and falling blood pressure. On several occasions during emergency surgery when gelatin solutions were used, the response of the patient was impressive.

Treatment of edema. It is in this field especially, where little is known about gelatin, that there is need for further investigation. Gelatin solutions have been effective chiefly in edema due to hypoproteinemia which may itself be due to many causes. The author has been successful at times in treating edema due to starvation, liver cirrhosis, and nephrosis, as well as several cases of terminal anasarca in lymphosarcoma and Hodgkin's disease. In the management of these problems, daily infusions of 500 cc. or 1,000 cc. of a 6 per cent gelatin solution were given, with a close watch on the serum albumin concentration. The use of mercupurin in doses of 2 cc. after several gelatin infusions has resulted in greater diuresis in certain cases than either mercupurin or gelatin solutions alone. Because of the increase in blood volume which follows gelatin infusions, its use should be avoided in patients with edema of cardiac origin. The large molecular gelatin produces greater diuresis than the small. In several instances, administration of the small molecular gelatin has been followed by an increase in weight. The gelatin concentration of edema fluid has been found to be greater after infusion with the small molecular material than with large molecular gelatin. We have been asked if gelatin has an effect on pleural effusions or abdominal ascites. No such hope was entertained and no beneficial effect has been seen, although peripheral edema associated with either of these conditions may be benefited.

The chief precaution to be observed in the use of gelatin solutions is one suggested by the circulatory

changes after gelatin infusion. The 6 per cent gelatin solution has twice the oncotic pressure of plasma, and, therefore, must be used with caution in patients of doubtful cardiac status. It should not be used at all in patients with any signs of cardiac failure, no matter how slight. As it has been shown, the maximum blood volume increase occurs three hours after infusion and for that reason cardiac decompensation may occur some hours after the close of an otherwise uneventful gelatin infusion. Paradoxically, the availability and low cost of gelatin solutions are in themselves sources of potential danger, for without need of blood donors or the necessary formality of obtaining plasma from the plasma bank, the clinician has a large supply of a powerful agent ready for immediate and continued use. If the limitations of gelatin solution are kept in mind and it is used with the same judgment and precaution as plasma and for similar indications, it will prove an effective plasma substitute.

BENJAMIN GOLDMAN, M.D.

RETICULOENDOTHELIAL SYSTEM

Fotheringham, W. T., and Sugasti, J. A.: The Importance of Roentgenology in the Diagnosis of Traumatic Ruptures of the Spleen (Importancia de la radiologia en el diagnostico de las ruptures traumaticas del bazo). *Rev. As. méd. argent.*, 1944, 58: 913.

Traumatic ruptures of the spleen without an open wound of the abdomen are extremely rare. Only 8 have been seen among 3,500 admissions to the Emergency Surgical Service of the Public Welfare Hospital of Rosario.

Unless the hemorrhage is very profuse and floods the peritoneum at once, there is generally a latent period during which the clinical symptoms are slight and indefinite. It is during this period that diagnosis should be made in order that surgical treatment can be effective. The only means of making an absolutely certain diagnosis is by roentgen examination. If the possibility of rupture of the spleen is suggested by pain in the left hypochondrium irradiating to the shoulder of the same side a simple screen examination without contrast should first be made with the patient standing. This will show an abnormal opacity at the bed of the spleen which pushes the left diaphragm up and renders it immobile. The great tuberosity of the stomach is pushed toward the midline and the air chamber is reduced in size. The splenic angle of the colon is pushed downward and inward. An examination with contrast medium is then made which confirms the changes in the air chamber of the stomach and shows others in its middle part, a characteristic image.

The diagnosis can be confirmed absolutely by the injection of about 1,000 cc. of air followed by screen examination. This shows the spleen in the greatest detail, particularly its upper pole; its base passes into an opacity which shows a fluid level extending from the lateral surface of the spleen to the ribs. Sometimes there are other fluid levels in the right hypochondrium. If the patient is moved slightly there is an unmistakable wave in the fluid level. These changes should be recorded on roentgenograms.

The authors describe 6 cases in which they made the diagnosis by means of roentgen examination and present the roentgenograms. In 3 other cases in which pain in the left hypochondrium suggested traumatic rupture of the spleen roentgen examination proved that it did not exist.

AUDREY G. MORGAN, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Moore, T.: Underwater Blast Injuries of the Abdomen. *Brit. M. J.*, 1944, 2: 626.

The basic mechanism of underwater blast injuries to the abdomen is still uncertain. This article is based on the treatment of 18 patients, 9 of whom were subjected to operation. There were also 22 other patients who were examined and questioned, and kept under observation after having been operated upon elsewhere.

In underwater blasts there is no after-wave of negative pressure, thus the abdomen is affected more than the thoracic cavity. The shock of the explosion on the abdomen may be described as being like a severe kick or a viselike tightening, as though the abdominal contents were forced up through the body into the head, or as if a giant hand were squeezing the body from the waist downward. Many victims have the sensation of having the legs shot away. Several patients have had temporary paraplegia. None of the patients in the group described, complained of pain in the testes.

Following these painful symptoms the patients managed to swim, but after they had been picked up by another vessel they found they could not straighten themselves up or walk because of abdominal pain. After rescue there may be an urgent desire to defecate a blood-containing stool. Vomiting is a very common symptom.

Clinically these patients show all the signs and symptoms of a generalized, severe abdominal blow. Many die at once, or shortly after their injuries, from shock and hemorrhage. The clinical picture in those rescued varied according to the time which had elapsed since the injury, and the extent of the injury. The more severe the injury, the more severe the abdominal pain, vomiting, and shock.

The most important early factor in the diagnosis is to know whether intestinal perforation has occurred. The greatest attention must be paid to the local abdominal signs, the most important of which are tenderness and rigidity. Intestinal perforation may be simulated by intraperitoneal hemorrhage and by injury to the lungs.

The author places great reliance on the observation that if rigidity is caused by peritonitis due to perforation, the abdomen does not relax during expiration. Late perforations of the intestine may occur.

The most important lesions are hemorrhage and perforation. Hemorrhages may be of the scattered pin-point type, the linear subperitoneal, or the massive, irregular subperitoneal type. Perforations were found in the ileum and in the ascending and pelvic colon. Perforations varied from the size of a pin point to 3 cm. in diameter. Frequently there is only one perforation, but at times several may be found.

Various other hemorrhages and injuries to the internal organs are described. Gas-containing abdominal viscera are most commonly and markedly affected.

Any one within 200 yards of the explosion is in danger, and those facing the explosion are usually more seriously injured than those with their backs to it. Distance is the best safeguard against injury, and the safest position appears to be floating on the back.

Treatment consists of rest, warmth, morphine, and intravenous infusions of blood or plasma. Mask administration of oxygen is used for patients with chest lesions.

Late perforation must always be considered and appropriate measures taken. In cases of perforation, operation is performed as soon as the patient is fit for surgery. Spinal analgesia is suitable if shock has been overcome. Intravenous administration of pentothal sodium combined with local block are useful in these cases. One of the sulfonamides is used before the abdomen is closed. Ordinary suture of the colon is carried out and the peritoneal cavity is drained. Continuous gastric aspiration, and the intravenous administration of fluid and sulfonamides are extremely important postoperatively.

Nine of the 18 personal cases were submitted to operation. Perforations were found in 8 of the patients. There were 2 deaths and in these cases perforations of the intestinal tract and blast-lung were found. The mortality among the operative cases was 22 per cent.

The postoperative complications were peritonitis, purulent bronchitis, and acute obstruction of the small intestine. Two of the patients who had been treated elsewhere previously for perforation of the bowel, subsequently developed intraperitoneal abscess; another patient developed a subphrenic abscess. RICHARD J. BENNETT, JR., M.D.

Mitchell, G. A. G.: Infection in War Wounds. *J. R. Army M. Corps*, 1944, 83: 225.

Mitchell attributes the high incidence of infected wounds in military, as compared with civilian, life to: (1) the severity of the average battle wound; (2) the proportion of open or closed fractures and joint injuries, and the degree of bone and soft-tissue damage; (3) the soiled character of the soldier's skin and clothing; (4) penetration and perforation of the body cavities; (5) the presence of foreign bodies and their irritant nature; (6) the circumstance of exposure to excessive heat or cold, battle strains, and lack of food and drink; (7) the circumstance of immediate treatment on the battlefield; (8) the necessity of transporting many hundreds of miles over difficult country before the wounded reach hospitals, and delays in getting definitive treatment; (9) the difficulty of maintenance of strict asepsis under battlefield

conditions, and the risk of cross infection; and (10) infection from vectors such as flies.

Bacterial infection was of the mixed type in all except 6 of the cases observed, the most common combined infection being caused by streptococci and staphylococci, although other organisms were often present with these in the same wound.

Streptococcal infections usually proved more troublesome in the earlier stages and were more liable to produce signs of general intoxication, while staphylococci were more persistent and difficult to eradicate, and were present in a high proportion of the truly chronic wounds.

The bacteriologist can provide invaluable help, yet too much emphasis must not be laid on the laboratory findings and prevent definitive treatment.

The cautious assessment of laboratory reports is especially necessary when the clostridia group are considered. In the orthopedic cases, these organisms were present in 28 per cent of the wounds, but only 1 patient had true gas gangrene and he might have escaped this complication if his grossly lacerated and contaminated leg had not been encased in an unsplit, unpadded plaster, with consequent swelling and interference with the circulation. The presence of clostridia organisms should never by itself lead to a diagnosis of gas gangrene. The diagnosis can be made with certainty only on the clinical appearance and examination of excised portions of the affected muscle.

Infected war wounds, like any others, may become chronic. Every general hospital with many casualties always has its quota of chronic cases. Figures show that approximately 33 per cent of the wounds at the author's hospital were still unhealed after two months, but in three months the number had fallen to 19 per cent largely because the removal of sequestra in 7 cases led to healing of persistent sinuses. The wounds slowest to heal were the sequel of mine explosions, and most of those were heavily contaminated and contained multiple foreign bodies.

The causes of chronicity in war wounds are many and various, but possibly the two chief ones are the gross and extensive nature of the original injury and the fact that infection is often well established before the surgeon has a chance to prevent it.

There are other factors also. The area of skin loss may be so great that healing by natural processes must inevitably be a lengthy process. The patient may be debilitated and his resistance undermined by strain, exhaustion, loss of blood, or a virulent infection. He may have suffered from lack of proper food and water, and in a few cases there may be some constitutional disease, such as nephritis, which reacts unfavorably on the reparative powers.

STEPHEN A. ZIEMAN, M.D.

Neel, H. B., and Cole, J. P.: Gas Gangrene in Amphibious Warfare in the Pacific Area. *Am. J. Surg.*, 1944, 66: 290.

In 984 consecutive fresh battle casualties, there were 7 cases of gas gangrene. In all the cases, a gram-positive bacillus, morphologically and culturally identified as the clostridium welchii, was found. The incubation period varied from one and one-half to five days. The average time that elapsed between the injury and the appearance of the symptoms was two and thirty-five hundredths days.

The lower extremity was the site of the infection in 5 cases, and the upper extremity was involved in 2 cases. The wound in each case was large, deep, and irregular, and it involved muscle. In 5 cases, fractures were present, and in 1 case amputation had been done previously.

In nearly all of the cases, pain was the initial symptom. Two patients were delirious on admission to the hospital. Local swelling, discoloration, crepitus, and a foul odor are the early diagnostic signs. Evidence of toxicity appears late in the course of the disease. A persistent elevation of the pulse rate was present. The temperature was not a reliable index to the severity and extent of the infectious process. A low erythrocyte count and a low hemoglobin content were the most striking laboratory findings. In 1 case the diagnosis was confirmed by x-ray examination.

The treatment, both prophylactic and therapeutic, is primarily surgical. Early care of wounds and excision of devitalized tissue may reduce the incidence of gas gangrene. In 1 case, excision of the wound gave satisfactory results. In the remaining 6 cases, amputation was necessary. Wounds should be left open, and vaseline gauze should be placed in them. Spraying of the stump with microcrystalline sulfathiazole was the practice in the hospital ship.

In patients with wounds of the extremities which are obscured by casts, early diagnosis of gas gangrene is difficult. The patient should be questioned frequently concerning the presence of pain. The cast should be examined for the characteristic odor of gas gangrene; swelling below the cast should arouse suspicion.

Multiple transfusions of whole blood were found to be the most valuable single adjunct to surgery.

Two of the 7 patients died.

SAMUEL KAHN, M.D.

Hutchinson, D. F., and Chapman, H. R.: The Evacuation of Casualties from a Normandy Beach. *J. R. Army M. Corps*, 1944, 83: 209.

This article narrates in detail the plan employed in the evacuation, transportation, and disposition of casualties from the Normandy beaches during the initial stages of the invasion assault. This consisted in evacuation of all casualties by sea from each of the 3 British sectors. An organization known as the Casualty Evacuation Point was set up on or near to the beach; it collected the casualties in D.U.K.W.'s (ducks), and transported them to Landing Ship Tanks (LST) anchored at sea.

On D1 day the LST was beached and the casualties were loaded aboard after the ship had discharged its cargo of men and supplies. Sixty per cent of the casualties were evacuated in this manner.

Each LST accommodated 144 bed patients and 100 walking patients and evacuation fell into 2 classes according to the water tide—the "low tide," when loading was done directly onto an LST; and the "high tide," when it was done onto a hospital carrier anchored from 3 to 5 miles out from shore with the carrier's water ambulance or a Landing Craft Tank from a harbor 2 miles from the CEP.

Every patient sent to the Casualty Evacuation Point was seen by a medical officer on arrival, was given a meal or some tea, had his dressings adjusted, and was given whatever adjustment treatment might be required; also cigarettes and sweets. Here he could rest until evacuation was feasible, during which time his documents were checked.

The activity which received these patients was likewise well organized; there were 3 medical officers at the Reception Center on duty during the day and 1 at night. STEPHEN A. ZIEMAN, M.D

Murray, R. O., and Mossendew, N. A.: Embarkation of Casualties from a Beach-Head. *J. R. Army M. Corps*, 1944, 83: 215.

This article discussed the evacuation of casualties from a beach-head, describing in detail the various units employed. The plan of evacuation consists in having a Casualty Embarkation Point on the beach which collects the casualties and disposes of them principally by dispatching them to hospital crafts. These are of 2 types, the hospital ships and the hospital carriers. The latter are smaller and intended for short voyages only; consequently they have a less specialized staff than the hospital ships. Each of these vessels serve several beach sectors and are supplied by Landing Ship Tanks (LST), water ambulances (usually 6 in number), from the hospital ship itself, Landing Craft Tanks (LCT) with a capacity of 100 stretchers and 100 sitting patients, Landing Craft Infantry (LCI) with a capacity of 40 stretcher and 60 sitting patients, motor launches carrying 14 stretcher and 20 sitting patients, and Dukws, which are amphibious crafts carrying 9 stretcher patients.

When landing strips could be established evacuation by air was also employed; however, certain selected patients for whom air travel was considered dangerous were denied this form of transportation. These were patients suffering from shock, abdominal and thoracic wounds, acute abdominal conditions, recent severe hemorrhage (including hemoptysis and hematemesis), gas gangrene, chemical gases, lobar pneumonia, pneumothorax, angina pectoris, coronary occlusion (during first month of condition), and meningitis (during period of increased intracranial pressure). STEPHEN A. ZIEMAN, M.D.

Warren, J. H.: Reception and Evacuation: Notes on Administrative Problems Arising in a Large General Hospital (1,500 Beds) Acting as a Casualty-Clearing Station. *J. R. Army M. Corps*, 1944, 83: 220.

This article describes the administrative problems which arose during the time in which the unit in question functioned as a general hospital although its staff was limited to that of a casualty-clearing station. The clerical staff worked in 2 twelve-hour shifts although these were stretched on many occasions to shifts of fourteen or fifteen hours' duration.

The cases were received in a Reception Tent where documentation, assorting of patients, and exchanges of equipment were done. A convoy of 200 could be cleared in this manner within two hours.

After the convoy had been admitted the index cards were sorted and filed alphabetically.

When a patient was ready for evacuation a form was filled out; urgent cases were indicated with a priority label, also those requiring special handling, such as air patients and those with maxillofacial and head injuries. Clean x-ray films were included among the transporting records. The patients were then placed on evacuation vehicles, motor car or train ambulances, planes, or other conveyances, at which time all items were checked.

This system of recording by index cards has proved of inestimable value and was arrived at through trial and error. It has been modified according to circumstances, but its value is worth the extra trouble entailed. STEPHEN A. ZIEMAN, M.D.

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

Hamilton, H. H., Custer, B. S., and Kellner, A.: Pilonidal Cyst; An Analysis of 132 Consecutive Cases. *N. England J. M.*, 1944, 231: 757.

This analysis of 132 cases of pilonidal cyst calls attention to a method of preoperative grading which proved helpful in determining those cases suitable for primary closure. The preoperative classification of cases was as follows:

Grade 1. On examination the patient presents a sinus or sinuses and a palpable tumor, but there is no history of inflammation or discharge.

Grade 2. The patient presents a history of discharge and recurrent local tenderness and swelling, but not within the eight weeks prior to examination.

Grade 3. The patient presents a history of recurrent discharge or previous abscess formation requiring drainage.

Grade 4. The patient presents acute suppuration and abscess formation.

The series was thus divided as: grade 1, 45 cases; grade 2, 24 cases; grade 3, 45 cases; grade 4, 9 cases; and ungraded, 9 cases, of which 4 did not come to surgery, and the remaining 5 were treated by excision and packing.

Excision and primary closure were done in 43 grade 1 cases, with 1 failure (2 per cent); in 20 grade 2 cases, with 2 failures (10 per cent); in 19 grade 3 cases, with 10 failures (53 per cent); and in none of the grade 4 cases. Failure is defined as any primary closure that requires reopening, or that on follow-up examination shows tissue breakdown or evidence of recurrence. The procedure of Ferguson and Mecray with minor modifications was followed.

In 82 cases treated by primary closure, including the failures, the average time from operation to return to duty was twenty-five days. Excision and packing was done in 24 of the first 66 cases, and the average time of hospitalization was sixty-two days. Only 4 of the remaining 62 cases received this type of management, and the period of hospitalization averaged one hundred and two days. This procedure has been supplanted almost entirely by that of partial closure.

The technique of partial closure used by these authors was that of MacFee. This type of management was used in 11 cases, in 9 of which the cysts were of grade 3; in 1 the cyst was of grade 4; and in 1 of grade 1, this cyst being too large for complete closure. The average period of time from operation to return of the patient to duty was forty-five days.

The procedure of incision and drainage was limited to 7 cases of gross suppuration and abscess formation. Incision and drainage at the outset and careful use of cauterizing agents effects a cure in simple types of abscesses. Care is taken to excise the fistulous tracts at the time of operation, and the wound is loosely packed with sulfanilamide gauze for one week. After this, the wound is treated daily with Carnoy's solution and saline solution until a clean, granulating surface is presented. These patients were discharged to duty as healed in an average of twenty-seven days after operation.

It is concluded that grade 1 and grade 2 cysts may be satisfactorily closed by the modified Ferguson technique, with only rare failures and recurrences. Grade 3 cysts should not be closed primarily, since failure occurred in 53 per cent in the cases so treated. The average hospital stay of the 128 patients operated upon for all grades of pilonidal cyst (from date of operation to complete healing and return to duty) was thirty-five days. JOHN L. LINDQUIST, M.D.

Karpovich, P. V., Starr, M. P., and Weiss, R. A.: Physical Fitness Tests for Convalescents. *J. Am. M. Ass.*, 1944, 126: 873.

From an analysis of data presented it was found that three days after an acute fever of two and a half days' duration an AAF cadet can pass a physical fitness test equivalent to walking up to a height of 20 feet and down again in thirty seconds (approximately to the third floor of an average building). One and a half additional days after fever, the convalescent cadet can pass a physical fitness test equivalent to climbing up 200 feet and coming down in five minutes (approximately to the twenty-first floor). After three more days he can make a score of 75 on the Harvard test for discharge to full military duty. The use of the Harvard test score of 75 is reliable for discharge to full duty, since all of 271 cadets were able to carry on without relapse. Testing and participation in the physical training of the convalescent training program reduced hospitalization somewhat, definitely did not prolong illness, and insured adequate physical fitness for return to full military duty. From a small number of cases, results suggest that sedimentation rate (Westergren method) of the order of 24 to 55 mm. is not a contraindication to full participation in the hospital physical training program.

The clinical physical tests described in this article were used to assist medical officers in classifying AAF cadets convalescing from acute, uncomplicated upper respiratory diseases for participation in a gradual physical training program. Participation in the physical training program resulted in a sufficiently high degree of physical fitness for the return of the subjects directly to full military duty when discharged from the hospital. J. M. MORA, M.D.

Brunschwig, A., and Nichols, S.: The Retention of Intravenously Infused Gelatin. *Surgery*, 1944, 16: 923.

In recent years parenteral injection of nitrogenous nutriment has become feasible by virtue of the development of casein digests suitable for intravenous injection. Evidence has also been presented in support of the view that protein molecules (homologous plasma proteins) injected intravenously might be utilized for nutrition. The use of "complete" foreign proteins would not seem possible in view of their antigenic properties. However, certain samples of gelatin have recently been found to be suitable for intravenous injection in that after their administration no immediate reactions were produced (except in isolated instances and these were not serious), sensitization did not develop, and no later toxic effects were manifested. Gelatin, however, is an incomplete protein in that it lacks a number of the essential amino acids. As the sole source of protein in the diet, it will not permit normal growth and development of experimental animals.

In view of the tolerance of human patients to repeated intravenous injections of gelatin, and evidence that some of it is metabolized, studies were carried out by the authors in a series of 23 patients to determine how much of this material is excreted in the urine under the usual conditions of intravenous clinical administration. This question is of obvious importance because if most of the injected material is excreted unchanged in the urine, little opportunity for utilization will be afforded.

Twenty-three patients with various conditions received one or repeated daily intravenous injections of gelatin. In some instances the injections were made in the immediate postoperative period and the studies were carried out when the patient was receiving almost nothing by mouth. In others, the studies were carried out while the patient was partaking of the usual hospital diet.

As a result of their observations the authors present evidence to indicate that from 40 to 43 per cent of the gelatin injected intravenously in man as an 8 per cent solution in physiological saline solution is retained, as only from 60 to 57 per cent is recovered in the urine. The relative amount of gelatin retained is approximately the same whether 1 or 8 daily injections are made. Thus, the intravenous

injection of gelatin constitutes one method by which nitrogenous material may be administered to the organism.

It is not to be inferred that these studies are regarded as final evidence to justify the assumption that gelatin given intravenously is a protein food. Evidence of appreciable utilization has not yet been presented. Emphasis is placed only on the fact that protein in the form of gelatin may be administered to the organism with the retention of appreciable quantities of the gelatin by the organism.

JOSEPH K. NARAT, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Fleming, A., Young, M. Y., Suchet, J., and Rowe, A. J. E.: The Penicillin Content of the Blood Serum after Various Doses of Penicillin Given by Various Routes. *Lancet*, Lond., 1944, 247: 621.

Penicillin appears in the blood within a few minutes after an intramuscular or subcutaneous injection. From the point of view of getting the drug into the circulation, therefore, there is little to be gained by intravenous administration. Also the rapid rate of its disappearance from the blood is not markedly altered, whether the injections are given intravenously or intramuscularly.

The time at which measurable penicillin disappears from the blood is somewhat as follows:

Intramuscular dose	Time of disappearance
15,000 units	2 to 3
20,000 units	3
35,000 units	4
50,000 units	4 to 5
100,000 units	5 to 6

The maximum titer obtained in the blood after the injection of 15,000 units is necessarily much less than after the injection of 100,000 units; therefore, if the interval between injections is the same, the larger the dose the higher will be the average penicillin content of the blood. When single injections are used, however, a continuous bacteriostatic power can be obtained in the blood much more economically by the use of smaller doses. Six doses of 15,000 units given every two hours will certainly maintain a bacteriostatic power in the blood for twelve hours, whereas 100,000 units in a single dose will last only from five to six hours. However, there are times when injections cannot be given frequently; in such cases, the larger dose and less frequent injection are advantageous. There are times also when it is desirable to have a high concentration in the blood for only a few hours. If, for example, it is necessary to operate through septic tissues, a dose of 100,000 units given fifteen minutes before operation provides a high penicillin content throughout the operation and for an hour or two afterward, which seems to prevent any generalization or spread of the infection.

In hospitals, the most economical method of administering penicillin is by the continuous intramuscular drip. Even with a dosage of 60,000 units in twenty-four hours, the blood serum is rendered bacteriostatic, and with increased dosage it becomes much more highly bacteriostatic.

As yet, no decision can be made as to whether it is better to maintain a constant low level of penicillin in the blood, or to have a very high level for a short time after an injection, followed by a period of very low level before the next injection. Clinically, both systems work excellently.

SAMUEL KAHN, M.D.

Myers, R. S., Aldrich, R. H., Howard, R. W., and Walsh, R. A.: The Use of Gauze Inoculated with Penicillium Notatum or Impregnated with Crude Penicillin in the Treatment of Surface Infections. *N. England J. M.*, 1944, 231: 761.

In order to evaluate the use of gauze inoculated with penicillium notatum, pieces of 28-by-24-mesh absorbent gauze were folded to form eight thicknesses, cut circularly, placed in clean Petri dishes, and sterilized in a hot-air oven for one hour at a temperature of 400° F. Five hundred cubic centimeters of distilled water were placed in an Erlenmeyer flask, to which was added 6 gm. of dehydrated yeast and 12 cc. of glycerin. A separate mixture of 12 gm. of lactose, 12 gm. of cornstarch, and 30 cc. of cold distilled water was added. The contents of the flask was stirred well, and boiled for twenty minutes over a low flame. The Petri dishes and culture medium were cooled, and about 60 cc. of the medium were poured into each dish. A bit of the stock culture of penicillium notatum was then transferred to the plate with a flamed platinum loop. The dishes were placed in an incubator at a temperature of 23° C. The penicillin secreted during the growth process was deposited on the under surface of the gauze. Its concentration reached a maximum in twelve days and then rapidly retrogressed.

The plates containing the impregnated gauze maintained their potency for about two weeks when kept at a temperature of 5° C. or lower, and the crude penicillin liquor could be kept for about four weeks at a temperature of 5° C., without any appreciable loss in titer.

All cultures were insured against contamination.

Before the dressings were applied the lesions were prepared by cleansing them with an aqueous cationic detergent or with hydrogen peroxide. Gauze pads inoculated with mold or impregnated with crude penicillin liquor were then applied and held in place by adhesive tape or bandages.

Several cases of uterine cervicitis were treated also. In these, a pad of the mold-inoculated gauze or of gauze impregnated with crude penicillin was applied directly to the cervix. The dressing was held in place by a vaginal tampon for a period of thirty-six hours. With the exception of those on the uterine cervix, the dressings were renewed at intervals varying from one to four days. All of the patients were ambulatory, which made it difficult to change the dressings more frequently.

Forty-seven cases of surface infection were treated. Healing occurred in 25 and improvement was noted in 13 during treatment. The types of cases included leg ulcer, chronic endocervicitis, pilonidal-sinus wound, mastectomy wound, carbuncle, burn of the neck, peroneal wound, and ulcerative stomatitis.

Chronic or mixed infections did not respond so well as did acute infections, or infections of but one strain of a penicillin-sensitive organism.

Because of the difficulties associated with the preparation of crude penicillin and mold-inoculated gauze, the authors advise that only purified penicillin should be employed for the treatment of cases of surface infection. STEPHEN A. ZIEMAN, M.D.

Fauley, G. B., Duggan, T. L., Stormont, R. T., and Pfeiffer, C. C.: The Use of Penicillin in the Treatment of Peritonitis. *J. Am. M. Ass.*, 1944, 126: 1132.

Since peritonitis causes 92 per cent of all deaths in hospital patients admitted with a diagnosis of acute appendicitis, and it is also a frequent cause of death in ruptured peptic ulcer and penetrating abdominal wounds, the authors have prepared a controlled experimental study to ascertain the effectiveness of penicillin administration in controlling fulminating diffuse peritonitis.

They produced peritonitis in dogs by occluding the blood supply of the appendix by means of ligation of the mesenteric vessels and also of the base of the appendix and then giving 50 cc. of castor oil with the stomach tube. This type of peritonitis, with a bacteriological flora quite similar to peritonitis in man, has a mortality of approximately 100 per cent.

The authors picked dogs at random and divided them into three groups. The first served as a control. The second group, given the same supportive therapy as the first, was also given intramuscular penicillin therapy beginning one hour postoperatively and continuing every four hours until recovery ensued. The third group was treated similarly, except that the penicillin therapy was not started until twenty-four hours after operation.

The clinical symptoms following the induced gangrene of the appendix in the dog are similar to those observed in appendicitis in man. In the control group, 25 of 27 dogs (92.6 per cent) died of fulminating diffuse peritonitis in an average of fifty-seven hours. In the second group (penicillin starting one hour postoperatively) all 20 animals survived and at autopsy on the twenty-first day after operation no evidence of generalized peritonitis was present. The dosages used were 100 Oxford units per pound given intramuscularly every four hours to the first 5 dogs. Because of their critical clinical condition, the rest of these animals received 150 Oxford units per pound every four hours for the first thirty-six or forty hours, then the dose was decreased to 5,000 units every four hours for two or three days, then to a total of 5,000 units every eight hours for two or three days. Twenty-eight dogs which developed the operative complication of an internal fecal fistula died under penicillin therapy and were not included in these figures.

In order to ascertain the effectiveness of penicillin after the infection was well established, in the third group, treatment was delayed until twelve hours after operation when definite abdominal rigidity was present. Penicillin was given as outlined for the second group, with the result that 4 of 19 animals died, a mortality of 21 per cent. The authors believe that large initial doses of penicillin possibly could have prevented these deaths.

The authors believe that since adequate penicillin doses given early are remarkably effective in the control of experimental peritonitis in dogs, it is reasonable to assume that the similar peritonitis in man due to appendical rupture will be favorably affected by adequate penicillin therapy. The longer the penicillin therapy is delayed the less favorable the results will be and the larger the dosages should be. Since relatively large doses of penicillin with regard to the body weight were used in these experiments, the authors believe that initial doses of 22,500 units per hour or about one-half million units per day would be necessary for a man weighing 150 pounds. As no toxic symptoms were displayed in this experiment and no serious symptoms have been described after massive doses in man, it would appear that large doses of penicillin are innocuous especially in relation to the critical nature of fulminating diffuse peritonitis.

In acute appendicitis, the authors do not consider penicillin a substitute for early surgery based on sound surgical judgment, but they believe that its use may be indicated in such instances as (a) operations in which peritonitis is encountered or localized abscesses have been broken into, (b) operations on the large bowel or intestines when some soiling occurs, (c) following gunshot or traumatic injuries to the abdomen, or (d) aboard small ships or submarines and at isolated posts where adequate surgery is not available. ROBERT BIGELOW, M.D.

Burnett, W. E., Rosemond, G. P., and Caswell, H. T.: The Use of the "Sump" Drain in Peritoneal Infection. *Surg. Clin. N. America*, 1944, 24: 1316.

The objectives of surgical drainage are as follows:

1. To remove exudate which may contain harmful toxins, necrotic tissue, or living bacteria, or may cause mechanical interference with physiologic functions.

2. To allow ventilation and/or irrigation for combating anaerobes.

3. To produce by adhesions a limited space through which infectious material can be channeled at a subsequent time.

4. To indicate the type of exudate (blood, bile, and so forth) from a hidden source.

5. To avoid the accumulation of exudate in an unavoidable or potential dead space (in amputations of the breast, extremities).

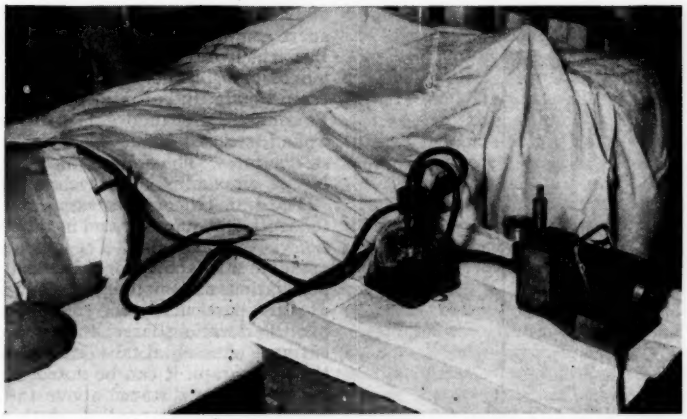


Fig. 1. A sump drain being used in generalized peritonitis. Note the exudate present in the bottle which has accumulated in eight hours. The abdominal dressing has not been changed in three days and is practically unsoiled. In actual practice the bottle and motor are on the floor.

Although only vaguely suspected at first, these principles have influenced doctors to utilize drainage for peritonitis since the infancy of surgery. Unfortunately, the same protective process of adherence and loculation which surrounds and incarcerates contaminated areas tends to defeat drainage by walling off into many compartments the irritated peritoneal cavity. Thus, a drain consisting of an irritant foreign material was even more quickly sealed off from the remainder of the cavity, often in a few hours.

Drainage in peritonitis is helpful in proportion to its efficiency. Gauze wicks tend to block drainage, unless the exudate is thin, and cause early firm adhesions. Rubber, of various compositions, is irritant and similarly is soon isolated. Drainage with such materials is of short duration, profuse amounts of exudate appearing for only a few hours. This has led to the search for less irritant materials which will not cause such rapid isolation.

In 1936, W. W. Babcock began seeking a drain of less irritant character which would increase the efficiency of drainage, more nearly approach the theoretical objective of the method, and would be less likely to cause dense insulating adhesions. First glass, and later stainless steel, fenestrated tubes were tried alone without gauze or other material about them. Inside each was a proportionately smaller tube, rubber at first, then stainless steel, connected to a motor-driven pump for constant aspiration of the pus which accumulated in these larger tubes, on the principle of a "sump," and this name was adopted for them.

In the treatment of peritonitis large quantities of exudate were withdrawn by this method in spite of operative aspiration. As much as from 100 to 200 cc. in each twenty-four hours for the first day or two has been recorded. Often fairly large amounts continue for three or four days. Instead of becoming thicker and more malodorous, as seen with older types of drains, the material soon changes from purulent to serous, the odor disappears with varying rapidity, and the serous fluid quickly diminishes in volume. This indicates absence of isolation and continued procurement of exudate as it forms. On several occasions the drains have been removed in two or three days because the patient's condition was excellent, peristalsis had returned, the graphic sheet was practically normal, and only a little serous drainage was obtainable.

In addition to the important factors of decreased mortality and morbidity according to the authors tabulated experience in 96 cases, other advantages of sump drainage are:

1. Removal of pus by positive means from the bottom of cavities instead of puddling and overflow from accumulation and body or intestinal movements as obtains with other methods. Thus even large but localized abscesses are more rapidly healed.
2. Frequent change of the small dressing is usually not required.
3. Ventilation and more adequate drainage decreases odor, which is an important esthetic factor to many patients.
4. Pus is collected in a bottle with or without deodorant or antiseptic for easy disposal instead of on the dressings, clothing, and bedding for general contamination of the patient and attendants.
5. Postoperative hernia is much less likely — 1 or 2 small hernias were discovered at reoperation for appendectomy although they were not demonstrable before incision.
6. Postoperative obstruction is less likely. Two of the 62 patients, or 3.2 per cent, were submitted to

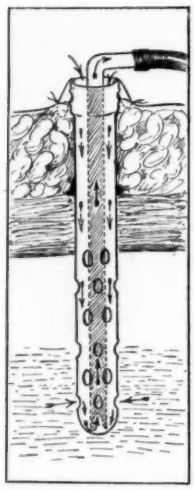


Fig. 2. Diagram of the sump drain. Note impossibility of direct suction on bowel or omentum provided there is a free airway between the inner and outer tubes. Note fish-mouth end of inner tube to avoid sealing.

ileostomy on the fifth postoperative day because of continued marked distention, but both had remained very septic and febrile, and the one on whom an additional blood count was taken showed continued leucocytosis. Both cases were interpreted as inflammatory rather than obstructive ileus, and both patients slowly recovered after ileostomy. Even when the condition is construed as being mechanical obstruction, its occurrence in 3.2 per cent of the cases compares favorably with the quoted statistics of 10 per cent and 7.4 per cent.

7. Postoperative secondary abscesses are rare. The one peritoneal abscess medial to the incision and two pelvic abscesses observed in these 62 patients occurred before the location of the drain was changed from right lower quadrant to the depths of the pelvis. Since this change, there has been no pelvic abscess formation.

In the extremely ill patients with diffuse peritonitis, shock is treated with plasma, blood, fluids, and adrenocortin. Without removal of the patient from bed, an anesthetic is injected in the right lower quadrant for a 3-cm. muscle-splitting incision. Through this a long sump drain is gently inserted into the pelvis, being guided into the cul-de-sac by a finger inserted into the rectum. The sterile assistant can then anchor the drain to the skin with wire suture. No other sutures are needed. A modified Ochsner treatment including constant gastric or intestinal suction, fluids, nutrition, and blood (given parenterally) is applied. Sulfonamides may be used systemically or omitted. Appendectomy can be done when the patient has recovered sufficiently, but not less than a week should elapse. For the average moderately ill patient, appendectomy is done under spinal anesthesia through a small muscle-splitting incision. Pus which can be reached without trauma is removed by aspiration. A sump drain is inserted into the pelvis to drain it and the right lower quadrant. Powdered sulfonamides may be applied and the wound is closed about the drain in layers with fine steel sutures. The drain is anchored to the skin with No. 32 wire and modified Ochsner treatment is used.

The drains themselves vary greatly in size both as to length and diameter and in the size of the perforations in the outer tube. The larger-sized perforations are more satisfactory for thick exudate. The smaller perforations are suitable in cases with a thin, watery exudate, particularly one composed of or containing bile. Perforations larger than 2 mm. may allow the entrance of omental tabs or even intestinal wall. In the photograph it can be noted that the drain protrudes a short distance above the skin level, even when dressings are applied. A thin, dry, gauze pad and a small aluminum cage is applied about this protruding portion which protects it from displacement by the bedclothes and from contamination, but does not interfere with the free passage of air down the outer tube as illustrated in the drawing.

Once the "sump set-up," consisting of drain, bottle, and motor, is connected, its care is quite simple. It is important to check the components of the unit for efficiency before it can be considered effectual. By clamping the tube to the motor and observing the rapid rise of the pressure gauze, one proves pump efficiency. By clamping the tube between the drain and the bottle the important fact that the bottle is air-tight can be determined by a steady rise of the vacuum gauge to the limit. Next the patency of the inner tube is checked by sudden release of this block. A characteristic "sump suck and gurgle" is heard as the built-up vacuum is opened to the abdominal portion of the drain. When there is abundant drainage the glass adaptor tube and bottle give visual evidence of function.

The most common difficulty encountered, namely, blocking of the inner tube by exudate, frequently can be discovered by simply walking by the patient's bed. The block results in a progressive vacuum, and the motor can be heard laboring to maintain the level. Further examination will show the vacuum gauge to have risen above zero, and the blocking off of the tube from drain to bottle with sudden release does not result in the characteristic suck and gurgle. This difficulty can be readily solved by removing and cleaning the inner tube or by inserting a new one. When the perforations of the outer tube become blocked due to drying and crusting of the slight residual exudate, it is usually time for the drain to be removed. However, if exudate is still present in the peritoneal cavity, an applicator soaked with peroxide and swabbed about vigorously within the tube often results in dissolution of these obstructing crusts, and further drainage may occur.

Removal of the drain is a welcome contrast to the usually difficult and often traumatic removal of

gauze and rubber drains. In most cases cutting of the wire suture and a gentle, steady pull result in a painless removal with no bleeding. On occasion omentum may enter the perforations and cause some drag with pain. Rotation of the drain will release these attachments. The small aperture in the incision decreases considerably on removal of the drain, and the tract remaining lends itself readily to catheter drainage for progressive shortening to avoid pocketing. In several patients whose drainage was never profuse or odorous, this step has been omitted.

The steel sump drain lends itself most readily to cleansing and sterilization. Sterile sets of these drains are kept in the operating room at all times for selection when needed. They are most durable and last for indefinite periods with a minimum of care. Any standard noiseless continuous suction motor is efficient.

The principles of the sump drainage technique are most important:

1. The drain is made of stainless steel and causes no demonstrable irritation to tissue.

2. It should be placed into the most dependent part of the infected cavity. The patient's position should promote gravity drainage of exudate into this dependent area.

3. Only liquid exudate is subjected to the vacuum. No direct suction is made at any time against bowel, omentum, or soft tissue unless dressings are erroneously allowed to seal the protruding end of the large tube. It is essential for proper functioning of the drain that there be free access of air and that there be sufficient space between the inner aspirating tube and the outer collecting tube to allow for its passage or else a vacuum against the bowel and omentum will occur.

4. Simple tests should be made frequently to insure proper function of the drain, bottle, and motor. If the vacuum gauge rises above zero, there is blockage.

BENJAMIN GOLDMAN, M.D.

ANESTHESIA

Cooper, W. G., II, Zumwalt, W., and Sugerbaker, E. D.: A Limited Comparison of Continuous Spinal and General Ether Anesthesia. *Surgery*, 1944, 16: 886.

A comparison is made of 100 consecutive patients receiving general ether anesthesia and 100 consecutive patients receiving continuous spinal anesthesia. One anesthetist gave all of the ether anesthesias and another gave all of the spinal anesthesias. The patients were essentially similar in both series, being indigent patients suffering from cancer with an average age of about sixty years and with many associated diseases other than the kind for which they were being operated upon. The relative consistency of all factors in both series, with the exception of the type of anesthetic used, made these series unusually good for comparative purposes.

It was noted that 44 per cent of the patients given ether anesthesia and 77 per cent of those given continuous spinal anesthesia were considered to have had satisfactory operative and postoperative courses. The incidence of hypotension was less in the spinal-anesthesia cases, and the occurrence of 3 fatal pulmonary emboli in the general-ether group alone seemed significant to the authors, who believed that the less complete relaxation produced by ether probably necessitated greater operative trauma. The technique of the continuous spinal anesthesia was described in detail. Routinely, a catheter was placed in the urinary bladder throughout the entire course of surgery. A stomach tube was inserted in patients in whom gastrointestinal surgery was planned and was permitted to drain throughout the surgical procedure. Oxygen was given intranasally when the anesthetic was given high in the spinal column, and ephedrine was used intravenously at the beginning of the operation and intermittently when needed during the operation. Certain modifications of the Lemmon technique and apparatus are enumerated.

The continuous spinal anesthesia seemed superior because of three factors: (1) there is complete and sustained relaxation; (2) it does not necessitate hurrying on the part of the surgeon; (3) it is especially advantageous in patients with cancer because of the element of uncertainty in all exploratory procedures in which the operability must remain in question until the peritoneum is open.

MARY KARP, M.D.

Hingson, R. A.: Continuous Caudal Analgesia: An Interim Report. *J. Am. M. Ass.*, 1944, 126: 1129.

The author reviews the status of continuous caudal analgesia on the basis of 42,000 parturients with comfortable labors and deliveries of babies born without narcotization and anesthesia. The average spontaneous breathing time of the baby from the moment the head was born was thirteen seconds, and the average lusty crying time was twenty-two seconds. The fetal mortality in this series was 1.7 per cent as compared with the fetal mortality of 5.2 per cent as registered for the entire United States. Sixteen maternal deaths occurred; 6 of these were attributed to obstetric complications, 7 to the misuse of caudal analgesia in unskilled hands, and 3 were considered anesthetic deaths.

The author condemns the use of this method for the relief of discomforts of preliminary and early labor, and advocates general anesthesia for the parturient in whom fear is uncontrolled.

The anatomy of the sacrum is reviewed. Malformations of the sacrum have been found to be more frequent than malformations of any other bone in the body.

The neurology of the cervix and uterus, from a study of 3,000 personally observed and managed obstetric cases, showed a natural anatomic dissociation between the motor and sensory components of the uterine nerves. Blocking of the eleventh and twelfth thoracic nerves was accompanied by total relief of abdominal cramps.

The three chlorides of Ringer's solution were considered the best diluent to intensify and prolong the

action of metycaine on the nerves in the peridural space.

The hypotension which may occur is combated by the use of 50 mgm. of ephedrine sulfate as needed, by the elevation of the extremities to be at right angles with the body, and by the use of 100 per cent oxygen inhalations. The occurrence of this hypotension is utilized in the pre-eclamptic patient, in the eclamptic patient with convulsions, and in the medical case with essential hypertension. In all of these types of cases striking clinical improvement occurred immediately after the institution of the caudal analgesia. This improvement was probably due to the peripheral vasomotor dilatation of the pelvis and lower extremities and the vasomotor changes in the kidneys, with an associated increase in the output of urine. The method is suggested for the treatment of thrombophlebitis, sciatica, intractable pain of pelvic carcinoma, ureteral and vesical colic, Dietl's crisis, burns of the lower extremity, arterial emboli of the legs, and peripheral vascular angiospastic diseases. It is also indicated in operations below the umbilicus in the debilitated, aged, cachectic patient, and in the management of industrial and war trauma of the lower half of the body.

One hundred and sixty cesarean sections have been performed under this method without loss of mother or baby.

The malleable stainless steel caudal needle has almost eliminated the hazard of needle breakage. The ureteral catheter has advantages for parturients who are unco-operative, and for those eclamptic patients who have lost motor control of their central nervous system. The continuous drip technique with modifications by Siever is mentioned. The latest modification is the author's introduction of the nontraumatic nylon needle which is inserted by means of a stiff steel stylet that is withdrawn as soon as the sacrococcygeal ligament is penetrated.

Emphasis is made on the newness of the continuous caudal analgesia technique, with a request for caution in its use. MARY KARP, M.D.

Hellman, L. M., Shettles, L. B., Manahan, C. P., and Eastman, N. J.: Sodium-Pentothal Anesthesia in Obstetrics. *Am. J. Obst.*, 1944, 48: 851.

Between September 1, 1940 and March 31, 1944, 1,415 deliveries were carried out at the Johns Hopkins Hospital, Baltimore, under sodium-pentothal anesthesia.

The amount of sodium pentothal necessary for low forceps delivery together with episiotomy and repair, lies between 0.75 and 1.0 gm. (from 15 to 20 cc. of a 5 per cent solution) provided that some form of sedation has been administered in labor such as a barbiturate or paraldehyde. For cesarean section 1.5 gm. (30 cc. of a 5 per cent solution) is the quantity usually required. The amount is never allowed to exceed 2 gm. Except in cases in which scopolamine has been given, atropine (0.5 mgm. or 1/130 gr.) is routine. Due to mechanical difficulties this anesthesia is not suitable for spontaneous deliveries.

TABLE I.—ANALYSIS OF 963 OPERATIVE DELIVERIES UNDER SODIUM-PENTOTHAL ANESTHESIA ACCORDING TO TYPE OF OPERATION

Low forceps	777	(80.7%)
Cesarean section	114	(11.8%)
Breech extraction	51	(5.3%)
Version and extraction	15	
Craniotomy	3	
Midforceps	3	

Although the relaxation of the abdominal walls provided by sodium pentothal is not sufficient for many abdominal operations, it is quite adequate for cesarean section. Bleeding is less than with gas-oxygen-ether, as is also, in the authors' opinion, postoperative distention. Except for versions on second twins, sodium pentothal is ordinarily contraindicated for this operation because the uterus does not relax well.

There is a period of five minutes after starting the anesthesia during which the amount of drug reaching the fetus is very small, and throughout the first ten minutes this amount is decidedly less, as a rule, than after fifteen or twenty minutes of the anesthesia.

TABLE II.—MG./100 BLOOD ACID PENTOTHAL IN MOTHER AND CHILD AT DELIVERY

Gm. of Sodium Pentothal given	Duration of Anesthesia in minutes	Mother MG./100	Infant MG/100
0.7	5	3.9	0.8
0.45	6	2.5	1.4
0.35	7	2.4	1.25
0.55	9	3.0	1.75
0.40	12	2.25	2.50
1.00	12	6.2	5.0
0.55	15	0.75	0.5

As far as the authors have been able to determine, there was no instance in the entire series of 1,415 cases delivered under sodium-pentothal anesthesia in which the anesthetic agent was directly responsible for an infant's death, or in which it played any demonstrable role.

It is the authors' impression that blood loss is less with sodium pentothal than with gas-oxygen-ether. The incidence of postpartum hemorrhage in the present series (600 cc. or more) was given as 2.8 per cent.

There were 2 maternal deaths in the series. Both patients were colored; they were nineteen and sixteen years of age, respectively; both were primiparas and both presented symptoms of severe toxemia of pregnancy.

Sodium pentothal has been employed successfully in approximately 500 additional obstetric operations not intended for immediate delivery of the infant—notably in puerperal tubal ligation, completion of incomplete abortion, artificial rupture of the membranes for the induction of labor, and manual removal of the placenta.

EDWARD L. CORNELL, M.D.

Hayman, I. R.: Experiences with Anesthesia in Combat Areas. *War Med.*, Chic. 1944, 6: 353.

The duties of the anesthetist in the combat area includes not only the administration of the anesthetic agents but preoperative and postoperative care of casualties.

Shock therapy of the casualty patient is discussed with the related derangement of the cardiovascular and respiratory system. Respiratory emergencies are enumerated including the relaxed tongue, foreign bodies, laryngospasm, tension pneumothorax, and open wounds of the chest. The immediate treatment of any condition that impaired tidal exchange included the administration of morphine tartrate in ¼-gr. doses; however, morphine was not given when head injury was possible or when increased intracranial pressure was evident. The use of oxygen or air under pressure, the intravenous injection of atropine, and intubation were the procedures of choice when laryngospasm occurred.

Tension pneumothorax is the result of a laceration of the the lungs and bronchi with the formation of a bronchopleural fistula. Treatment involves the reduction of the elevated intrapleural pressure and is most easily accomplished by the insertion of a short needle of wide bore.

It is important to recognize and treat the incipient insidious anoxia. A patient with slight anoxia may present a picture with symptoms of alcoholic intoxication, euphoria, ataxia, muscular weakness, impairment of muscular function, amnesia, and diminution of the special senses. The administration of oxygen by catheter or Boothby mask technique was used for this condition with gratifying results although the supply of oxygen which was available with the British in Tunisia was limited.

The available anesthetic drugs are outlined and the choice of an anesthetic agent is discussed. Pentothal sodium (given intravenously) was used far more than all other agents. It was usually necessary for the anesthetist to be responsible for several anesthesias going at the same time. For all abdominal operations anesthesia was induced with chloroform, ethyl chloride, or pentothal sodium followed by open or endotracheal ether-oxygen anesthesia. Most of the men with head injuries received treatment under local anesthesia. Spinal anesthesia was resorted to in only a few instances, as it was not considered suitable for battle casualties in the front lines; within a few hours after injury, one could not be certain of cardiovascular stability in spite of the apparent absence of shock. Block of the lumbar sympathetic ganglions was performed in only a few cases in an attempt to increase the peripheral circulation of the lower extremities; and blocks of the brachial plexus and of the median, ulnar, and radial nerves at the wrist were occasionally done for the surgical treatment of the arm and hand.

MARY KARP, M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Shelden, C. H., and Pudenz, R. H.: Improved Retractor for Hemilaminectomy. *Surgery*, 1944, 16: 884.

In order to obtain adequate exposure for successful removal of protruded intervertebral discs, Shelden and Pudenz constructed a retractor which facilitates hemilaminectomy. It consists of two blades of unequal lengths, the shorter having three long teeth which are inserted through the lumbar fascia adjacent to the spinous process. The longer blade is 2 inches wide, slightly curved, and has small laterally bent serrations on the free end; these permit fixation at any desired depth in the muscle. The two blades are attached to the arms of a Lilienthal rib spreader which allows exchange of blades.

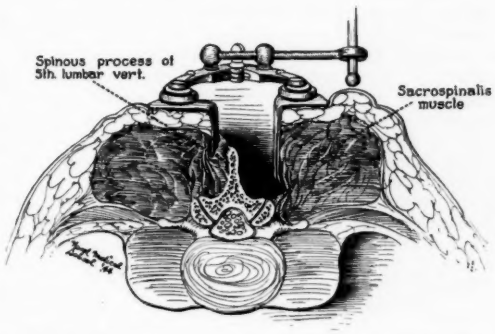


Fig. 1. Exposure for hemilaminectomy, demonstrating method of muscle retraction.

The practical use of the retractor is shown in the accompanying illustration. Hemilaminectomy is simplified and exposure improved, particularly in patients having strong muscles. The instrument is adapted for use in the cervical region.

STEPHEN A. ZIEMAN, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Gomez, G. E.: The Present Value of Roentgenology in the Diagnosis of Appendicitis. *Am. J. Roentg.*, 1944, 52: 624.

In this discussion on pathology of the appendix as determined roentgenologically, the author bases his remarks on chronic and recurrent appendicitis and observations made on 21,000 gastrointestinal examinations and conclusions reached by other writers.

The author's conclusions relative to appendical disease are reached after careful examination of the gastrointestinal tract and gall bladder, to eliminate these as the source of symptoms by careful and repeated examinations.

Having excluded the possibility of disease elsewhere he then searches for direct x-ray evidence of changes in the appendix, such as abnormalities in its size, shape, and position, and evidence of its physiological change such as its ability to fill and empty. The latter apparently has a direct bearing on its pathological state since an appendix which does not fill or delays in emptying itself is indicative of a disease process.

Indirect x-ray evidence of pathology is based on the reflex signs that can be elicited. These include pain over the appendix, pylorospasm which produces a six-hour gastric retention and tenderness on palpation of the pyloric area, aerogastria in six hours, increase in size and density of the liver shadow, and evidence of ileal spasm and ileocecal spasm.

On correlation of these findings with the clinical symptoms, the diagnosis of an active process can be determined. R. A. BERGER, M.D.

Oppenheimer, A.: Roentgen Diagnosis of Incipient Cancer of the Rectum. *Am. J. Roentg.*, 1944, 52: 637.

The author describes a technique for x-ray study of the rectum and sigmoid. In this procedure very small amounts of barium are employed and spot films or oblique films of the region in question can be made for the study of early lesions. While the method requires a little extra work the time consumed is not great and the results reward the extra effort.

A small rubber catheter is inserted into the rectum and, with an attached syringe, controlled amounts of barium are gradually injected into the rectum to a desired filling. After roentgenoscopy and filming the catheter can be connected to the regular enema apparatus for further filling and study of the colon.

By this method the author has been able to discern small lesions of the rectum, particularly small malignant ulcers which would otherwise have been overlooked. Likewise, other intraluminal and extraluminal lesions, which would be obscured by the regular massive filling of the rectum, can be found and differentiated. R. A. BERGER, M.D.

Vaughan, W. W., and Eichwald, M.: Priodax; A Contrast Medium for Cholecystography. Analysis of 163 Cases Outlining the Various Reactions in 3 Techniques and the Operative Findings in 22 Cases. *Radiology*, 1944, 43: 578.

Cholecystography is a routine procedure in the study of gall-bladder disease. The high accuracy of this procedure (95 per cent) emphasizes the clinical importance of this study.

Since the original work of Graham and Cole on gall-bladder visualization by intravenous injection of tetrabromphenolphthalein, science has been striving constantly to improve the method by use of various chemicals and techniques. Tetraiodophenolphthalein was substituted for tetrabromphenolphthalein less than one year after the original (Graham-Cole) publication and remained the chemical of choice until the recent advent of priodax.

The clinical use of priodax (biliselectan, as it was called in Germany) was first described by Kleiber in 1940; this dye was used on 55 patients and the results were verified by surgical exploration. In addition to the fact that it was an excellent contrast medium, it minimized the extent of diarrhea, nausea, and vomiting.

Priodax is a white, odorless powder, soluble in alkali, ether, alcohol, and acetone, but almost insoluble in water. Experimental studies showed that the lethal dose with oral administration was 1,000 mgm. per kilogram of body weight. Fifty per cent of the priodax used is excreted through the urinary tract, in contrast to the 10 per cent of tetraiodophenolphthalein when the latter is used. The remainder of the tetraiodophenolphthalein is excreted through the gastrointestinal tract, which is undesirable from a roentgenographic viewpoint. Priodax is available in tablets of 0.5 gm. each; the dosage is 1 tablet per 25 pounds of body weight. Tablets should be swallowed with or without fluid, but should not be chewed.

The authors report a series of 163 cases in which priodax was used. The single-dose method was used in 51 cases; a divided dose was given in 55, and a double dose in 57 cases. The usual preliminary preparations were followed. In the single-dose method, 6 tablets were given following the fat-free evening meal; in the divided dose, 3 tablets were given following the noon meal and 3 following the evening meal; in the double dose, 6 tablets were given after the noon and evening meals.

Toxic effects with the use of priodax, given by the various methods, were infrequent and minimal in comparison with those following the use of tetraiodophenolphthalein. Roentgenologically, the gall-bladder shadow was a little more dense with the use of the double-dose method; however, it was satisfactory in all methods. For purposes of economy and standardization, the single-dose method is used.

In 22 of 226 examinations, surgery confirmed the roentgen findings of a pathological gall bladder. In 1 instance of nonvisualization of the gall bladder, a normal gall bladder was found at surgery. This patient, however, had clinical jaundice with an icteric index of 44. MAURICE D. SACHS, M.D.

Heublein, G. W.: The Roentgen Diagnosis of Traumatic Lesions of the Cervical Spine. *J. Am. M. Ass.*, 1944, 126: 950.

The author reports on the newer developments of apparatus and technique at the Percy Jones General Hospital, Battle Creek, Michigan, which permit an accurate roentgen diagnosis of traumatic lesions of the cervical spine, and includes several valuable illustrations to prove his statements.

The acquisition of the Morgan meter, which is not as yet in general use, has helped considerably in the making of good roentgenograms of both simple and difficult projections of the cervical spine. The operation of the meter depends on the fact that intensity × exposure time = a constant. Thus if the intensity reaching the film is known in advance, the time for proper exposure can be read off directly from a calibrated scale on the meter. By this method excellent roentgenograms can be obtained even through heavy plaster casts.

In addition to routine anteroposterior and lateral films at a distance of 6 feet, roentgenograms are being made through the open mouth in oblique (from 50 to 55 degree) projection, and in the Jackson position, similar to an exaggerated Waters position which is used in the examination of the paranasal sinuses.

In this institution, fractures of the cervical spine comprise 23 per cent of all spinal fractures. They are of two types: (1) those which affect the cord-protecting portion of the spine, i.e., the neural arch and its processes; and (2) those which affect the weight-bearing structures of the spine, i.e., the vertebral bodies. The latter vary from minute spicules projecting anteriorly or as a moderate bulge along the anteroposterior border of the body to considerable compression of the spongy portion. Dislocations are observed with or without fracture, in sharp contradistinction to the dorsolumbar spine where dislocations almost invariably are associated with fractures. Soft-tissue swellings adjacent to the vertebral bodies are also found to be of significance as they indicate hemorrhage, edema, or infection. In fractures of the arches, callus formation often constitutes the most prominent feature.

Certain special procedures are also stressed by the author. Thus, in not a few of the cases it is advisable to make roentgenograms in the lateral view with the neck in flexion and extension. Exposures made in flexion may show a subluxation not demonstrable in conventional views. In other instances, delayed roentgenograms serve a better purpose. This applies especially to the fractures running through the base of the odontoid process, which may be completely missing at the initial examination but may be revealed some weeks later, after a rarefying osteitis has developed along the fracture line. Injuries to the intervertebral discs are often advantageously demonstrated by pantopaque myelograms. Successful delineation of such lesions, however, is not always an easy task.

Accurate diagnosis depends on several important factors, such as (1) proper apparatus, including canvas support and a special attachment for obtaining lateral films in the prone decubitus, (2) adequate extension of the neck to prevent escape of the opaque material into the basal cisterns, (3) experienced spinal puncture, a factor which cannot be too strongly emphasized, (4) proper withdrawal of the opaque medium at the end of the examination, to be checked by a scout film of the area examined, and (5) the closest correlation of the clinical and roentgenographic findings.

The general conclusion is reached that the roentgen examination is an invaluable aid in the diagnosis and differential diagnosis of traumatic lesions of the cervical spine. T. LEUCUTIA, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Najjar, V. A., Holt, L. E. Jr., and Royston, H. M.: A Note on the Minimum Requirements of Man for Vitamin C and Certain Other Vitamins. *Bull. Johns Hopkins Hosp.*, 1944, 75: 315.

A group of 7 young adults were given for a period of eighteen months a diet in which all water-soluble vitamins were provided as pure principles in carefully measured quantities. With the exception of thiamine, the intake of which was gradually reduced until deficiency symptoms appeared, the vitamins were in quantities which did not vary throughout the entire experimental period. No symptoms of any deficiency other than that of thiamine were observed. These experiments do not define the minimal requirements of these factors, with the exception of thiamine, which is discussed elsewhere. They do, however, establish upper limits for the minimal requirement. Of particular interest are the observations on ascorbic acid, which confirm those of Pijoan and Lozner that scurvy does not develop on a daily intake of from 18 to 25 mgm. of ascorbic acid.

Ruffin, J. M., Cayer, D., and Perlzweig, W. A.: The Relationship between the Clinical Picture of a Mild or Early Vitamin Deficiency and Laboratory Determinations of Vitamin Levels. *Gastroenterology*, 1944, 3: 340.

The frequency of full-blown vitamin deficiencies such as beri-beri, pellegra, and scurvy is decreasing rapidly and they no longer constitute a serious problem in North Carolina. It is reasonable to assume that for every advanced vitamin deficiency there must be many mild or early avitaminoses. It is difficult to determine whether one is dealing with a patient having a true vitamin deficiency or only a constitutionally inferior individual. Correct diagnosis is of greatest importance then for the intelligent use of vitamin therapy.

Recently laboratory procedures for measuring vitamin levels in the blood and urine have been devised and standardized. The application of these procedures in diagnosis may be extremely valuable if the patients with unquestionable evidence of vitamin deficiency prove to have significantly lower levels than normal controls. The authors undertook this study in an effort to determine if there was a relationship between early clinical vitamin deficiency and the laboratory determination of vitamin levels.

Two groups of patients were selected. The first, with vitamin deficiencies, were patients with glossitis, papillary atrophy of the tongue, cheilosis, or peripheral neuritis who showed the most reliable evidence of B-complex deficiency. All 26 patients selected gave a history of an inadequate diet and one or more of these findings. All were ambulatory, free of organic disease, and without a history of recent vitamin therapy.

The second group were the controls who were again divided into 2 groups: (a) patients with no definite evidence of a deficiency state and who ate the usual diet of an average tenant farmer. They presented a variety of neurasthenic complaints and represented constitutionally inadequate individuals with organic disease; and (b) normal students, technicians, and dietitians, all of whom had been subsisting on an apparently adequate diet.

In evaluating the vitamin tests the figures comprising the lowest 10 per cent of the normal control group were arbitrarily selected as being the *suggested lower limit of normal values* since there was little agreement in the literature as to what constitutes the lower limit of normal.

The laboratory examinations for determining vitamin levels were carried out on blood plasma for vitamins A, C, and carotene. B-complex vitamins were determined in the urine before and after a test dose, by chemical or biological assay.

The distribution of vitamin A and carotene levels showed a statistically significant difference between the normal controls and the deficiency group with the ward controls falling midway between the two. Although no clinical evidence of an A deficiency was observed in any patient, this study indicated that low levels of plasma vitamin A and carotene are likely to occur in patients in this locality with a mild deficiency of B complex.

The vitamin C values showed a wide discrepancy between the suggested lower limit of normal (0.15 mgm.) and the generally accepted value of 0.6 mgm. Nearly 50 per cent of the normal controls had values of vitamin C which fell below 0.6 mgm., and the authors believe this value is possibly too high. The higher vitamin C values are more apt to occur in normal individuals, but the distribution was so wide that there was no statistical significance between the two groups.

There were striking statistical differences between the two groups observed in the urinary excretion levels of nicotinic acid, riboflavin, and thiamin, the greatest variations being found in nicotinic-acid levels. There was little difference in the pyridoxine values of the two groups, which suggested that pyridoxine deficiency is not likely to occur in B-complex deficiencies, a point in keeping with the authors' clinical impression.

Most patients in the deficiency group had levels below the suggested lower limit of normal in more than one vitamin (22 of 26 when the B complex alone was considered, and 24 of 26 if vitamins A and C and carotene are included). Twenty-four of 26 patients classified clinically as having a B-complex deficiency had levels below the suggested lower limit of normal in nicotinic acid, riboflavin, or thiamin.

It appears then that patients having clinical evidence of a deficiency state based on the criteria enumerated are very likely to have levels which fall below the suggested lower limit of normal in one or more members of the B complex. If observations made in this study are confirmed by subsequent study, laboratory determinations may become useful procedures in the recognition of early deficiency states. ROBERT BIGELOW, M.D.

Volpitto, P. P., Woodbury, R. A., and Abreu, B. E.: The Influence of Different Forms of Mechanical Artificial Respiration on the Pulmonary and Systemic Blood Pressure. *J. Am. M. Ass.*, 1944, 126: 1066.

An improved technique has been developed for the measuring of the effective pulmonary and the effective systemic blood pressure in animals with a closed chest. The pulmonary and systemic blood pressures have been recorded while respiration was maintained with the individual use of seven resuscitators.

One sound was inserted into the exposed left carotid artery, on into the aorta, past the semilunar valves, and into the left ventricle. The other sound was inserted into the exposed external jugular vein down to the superior vena cava and right auricle into the right ventricle.

Cardiac arrest was produced (1) by complete occlusion of the airways in 3 dogs; (2) by use of the helium with carbon-dioxide-absorption technique in 2 dogs; and (3) by electrically induced ventricular fibrillation in 2 dogs.

No matter what method of mechanical artificial respiration was used, recovery of the animal was accomplished when respiratory arrest and slow, weak cardiac contractions were produced by the administration of helium with the carbon-dioxide-absorption technique. No significant change was produced in the pulmonary and systemic blood pressures with any of the methods of resuscitation studied.

Any blood flow produced by the resuscitators did not reach the coronary and cerebral arteries. On the other hand, blood was pushed toward the extremities and cutaneous areas.

Intrapulmonic positive pressure greater than 10 or 12 mgm. of mercury, if maintained for a prolonged period of time, may hinder venous return to the right side of the heart.

RICHARD J. BENNETT, JR., M.D.

Henry, F. M., Lawrence, J. H., Bridge, E. V., and Williams, O. L.: Protective Effects of Preoxygenation on Abdominal Gas Pain; Results of a Study of Preflight Breathing of Oxygen on Pain Resulting From Decompression to 38,000 Feet. *War Med.*, Chic., 1944, 6: 395.

The denitrogenation resulting from the breathing of oxygen has been reported to relieve postoperative and obstructive abdominal gas distention in human beings and has been found to reduce the total amount of gas in an isolated intestinal loop in dogs. Radioactively labeled inert gas introduced into the stomach and lower part of the bowel of human subjects is excreted by the lungs in proportion to the pressure gradient. Swallowed oxygen would be expected to cause less trouble than swallowed air because of its additional metabolic elimination. In view of these observations, it occurred to the authors that the incidence and severity of pain due to the expansion of gas in the digestive tract resulting from decompression in an altitude chamber or in an aircraft flight might be reduced by the preflight breathing of oxygen.

A control series of 80 healthy young males was decompressed twice to 38,000 feet and exercised at that altitude for ninety minutes. Breathing of pure oxygen began nine minutes before the altitude was reached. A similar group made three ascents under the same conditions except that the breathing of oxygen began one-third hour, one hour, and two hours before the altitude was reached; 61 of these subjects made all three ascents.

In 29 per cent of the controls definite gas pain developed; with prebreathing of oxygen for one-third hour the incidence dropped to 23 per cent, with one hour it was 19 per cent, and with two hours, only 10 per cent. Moderately severe gas pain occurred in 8.4 per cent of the subjects in the control runs, in 5.8 per cent in the one-third-hour runs, and in 2.7 per cent in the one-hour preoxygenation runs. No pain of this or greater severity occurred with two hours of preoxygenation.

Detailed examination of the data yields no evidence that differences in decompression experience, diet, or elapsed time between meals and ascent can account for the observed protection.

Definite gas pain appears to have a higher incidence if decompression occurs three hours after eating than is the case if the elapsed time is only one or two hours.

It is concluded that two hours of preoxygenation causes a decided reduction in the incidence and severity of abdominal gas pain resulting from decompression to 38,000 feet (11,400 meters).

JOHN E. KIRKPATRICK, M.D.

Kritzler, R. A.: Acute High-Altitude Anoxia; Gross and Histological Observations in 27 Cases. *War Med.*, Chic., 1944, 6: 369.

Fatalities in air crews, due to deprivation of oxygen during bombing operations at high altitude, have afforded an opportunity to study the gross and microscopic anatomy of acute anoxia in man as it occurs at a low atmospheric pressure.

In 1942, Mueller and Rotter described 4 cases of acute high-altitude anoxia among air crews of the Luftwaffe. They found congestion of all organs of the greater circulation, which they attributed to right ventricular failure and to peripheral vascular collapse. In all cases these authors noted an absence of clotting of the blood. Fat-free vacuoles, either optically empty or partially filled with refractive granules staining lightly with eosin, were present in

the livers of all patients. In heart-muscle cells the vacuoles were observed to be adjacent to and deforming the nuclei, and they were frequently arranged in continuous strands appearing as a "string of pearls." The vacuoles were considered similar to those described by Pichotka, Hesse, Ladewig, and Trowell.

Twenty-seven autopsies were performed during 1943 in one hospital on members of high-altitude bomber crews in whom death had been attributed to anoxia by the Air Force medical officers who investigated the cases. In no instance was the analysis of the history complicated by the presence of wounds. In no case was a rapid ascent to high altitude recorded. Although the possibility of fatal air embolism was not considered likely at the altitude at which death occurred, a search for intravascular gas in the right ventricle and in the mesenteric veins was made in 16 successive cases. None was found. In general the casualties occurred at altitudes of from 24,200 to 31,500 feet (7,200 to 9,450 meters), but in many instances the precise level at which difficulty was encountered could not be determined because the exact time of death was not always known by crew mates.

A study was made of the findings at autopsy in 27 cases of acute high-altitude anoxia. Widespread, severe capillary congestion was found. This was conspicuous and most constant in the pulmonary, renal, intestinal, and cerebral capillaries. The skeletal muscle did not have this congestion. In a high proportion of cases the systemic venous and the portal circulations showed gross and microscopic congestion, and the right ventricle was dilated. There was wide individual variation in the incidence, location, and amount of edema and hemorrhage. An exception to this was the consistent occurrence of hemorrhage in the thymus and in the middle ears. Swelling of the endothelial cells of capillaries of the renal medulla was observed. The presence of fat-free and glucogen-free vacuoles, previously described, in the myocardium and liver, and less frequently in cells of other organs, was confirmed. These vacuoles occurred with equal frequency in cases of anemic anoxia (acute carbon-monoxide poisoning), but were rarely found in the tissues in nonanoxic control cases.

JOHN E. KIRKPATRICK, M.D.

Brues, A. M., and Shear, M. J.: Chemical Treatment of Tumors. Reactions of 4 Patients with Advanced Malignant Tumors to Injection of a Polysaccharide from Serratia Marcescens Culture Filtrate. *J. Nat. Cancer Inst.*, 1944, 5: 195.

Certain preparations of bacterial origin, when administered parenterally to animals bearing sarcomas, produce hemorrhage in the tumors within a few hours. The action is highly selective, for while severe hemorrhage is induced in the tumor, it has not been reported to occur in any of the normal tissues, with a few minor exceptions of slight degree. The hemorrhage and necrosis produced in this way are followed, in some instances, by complete and permanent regression of the tumor.

The bibliography on the treatment of human tumors with induced bacterial infections or with bacterial products began about seventy-five years ago. Interest in the effect of bacterial preparations on tumors in experimental animals was revived in 1931 by the report of Gratia and Linz. Because of the high toxicity of such bacterial preparations, Shear and Andervont separated the active agent from toxic and inactive constituents; they obtained a polysaccharide fraction from filtrates of cultures of serratia marcescens (bacillus prodigiosus), one of the organisms used in the preparation of "Coley's mixed toxins."

This product was used by the authors in 4 patients with advanced malignant tumors (prostatic carcinoma, lymphosarcoma, multiple myeloma, and Ewing's sarcoma) in the form of muscular injections. All of the patients died with tumors. Two patients showed noteworthy relief of their symptoms. Two showed evidence of hemorrhage in the tumors at postmortem examination, although it was not possible to decide whether this finding was related to the treatment. The patient with multiple myeloma showed no evidence of any effect of this agent on the tumor.

Following initial chill and fever, a prolonged period of hypotension, sometimes with anuria and cardiac decompensation, occurred. Some of these reactions may have been the consequence of rapid absorption of products of destruction of the tumor tissue.

The 2 patients showing symptomatic relief also showed chemical evidence of the rapid breakdown of nitrogenous substances. This fact suggested that tissue protein, including nucleoprotein, might have been destroyed.

The findings in this preliminary study do not warrant the conclusion that this polysaccharide should be recommended in the treatment of patients with malignant tumors. The reactions in 2 cases, taken in conjunction with the results of animal experimentation, suggest that further investigations may yield interesting results. However, great caution must be exercised even in the experimental employment of this material in patients. Small doses may provoke violent reactions, and death may follow in a short time unless precautions are taken to counteract the undesired responses.

JOSEPH K. NARAT, M.D.

GENERAL BACTERIAL, PROTOZOAN, AND PARASITIC INFECTIONS

Hodges, R. G.: The Use of Sulfadiazine as a Prophylactic against Respiratory Disease. *N. England J. M.*, 1944, 231: 817.

In this experimental problem in which sulfadiazine was used as a prophylactic measure against respiratory diseases, the author had somewhat of an ideal condition for experimentation. The two groups of individuals used for controls and studies had been observed over a period of time before the experiment, and lived under similar environmental circumstances.

Since these groups were under close supervision the date obtained is worth consideration.

The effect on total respiratory disease after the administration of 2 gm. of sulfadiazine per day reduced the incidence to one-third and one-half of the control group. Throughout the experiment a variety of dosages were tried. No definite amount is recommended but an optimal amount for a given group should be worked out individually. No serious untoward reaction occurred in this study.

The most striking effect was obtained in streptococcal sore throat and scarlet fever in which the incidence dropped to zero.

In pneumococcal infections there was a significant drop, but since there was also a decline in upper respiratory infections the drop was hard to evaluate. Atypical pneumonia, likewise, displayed a low incidence but the number of cases were too few for significant analysis.

Acute rheumatic fever was less prevalent during this study and fell below the expected rate.

R. A. BERGER, M.D.

DUCTLESS GLANDS

Broders, A. C., and Parkhill, E. M.: Diffuse and Adenomatous Goiter and Goiter Induced by Various Agents. *Surgery*, 1944, 16: 633.

The diffuse colloid goiter, which used to be observed frequently from prepuberty to late adolescence, according to Haines is rarely observed today by the clinician. Furthermore, it is almost never seen by the surgical pathologist.

Since the advent of administration of a compound solution of iodine, the typical meaty exophthalmic goiter is seen much less frequently and has for the most part been replaced by a gland comparable to a colloid goiter, although smaller. The change in the exophthalmic goiter also is undoubtedly attributable to administration of the compound solution of iodine. Following the administration of a compound solution of iodine, the epithelium changes from columnar to a low cuboid or flat type and the acini dilate or at least have larger lumina, and their colloidal content is increased. This increase in the size of the lumina is probably the result of the diminution in the size of the cells. Some exophthalmic goiters, on the other hand, are more or less resistant to the changes that usually take place after the administration of a compound solution of iodine.

The nodules sometimes observed in hypertrophic parenchymatous thyroid or exophthalmic goiters with or without adenomas differ from the true adenomas of exophthalmic goiter in that they are not encapsulated, rarely contain true fetal acini, and under the microscope usually resemble the extranodular part of the goiter. In other words, the nodules are to a large extent comparable to the nodules observed in hyperplasia of the prostate gland.

In all hypertrophic parenchymatous thyroids or exophthalmic goiters, that is, in the diffuse nonnodular, the nodular, and the adenomatous types, varying degrees of chronic thyroiditis may be present. The chronic thyroiditis in these goiters is characterized by fibrosis and lymphocytic infiltration of the interfollicular tissue, with or without the formation of germ centers. This inflammatory reaction is probably attributable not to bacterial activity but to toxic products of the goiter. To some extent this form of thyroiditis may be activated by a compound solution of iodine, as it has been more in evidence since the therapeutic use of such a solution of iodine began.

Adenomas may occur singly but usually they are multiple. They vary markedly in size, in consistency, and from a light amber to a reddish brown in color, and they are encapsulated. They may undergo various types of degeneration, such as hemorrhagic, fibrous, hyaline, calcareous, lipoid (granular), and cystic. Macroscopically and microscopically, true adenomas differ from the surrounding thyroid tissue.

In recent years certain interesting and important forms of goiter have been observed after the administration of a variety of agents. Some of these goiters are now coming to the attention of the pathologist.

One of the first of these forms of goiter to be noted in man was that seen in patients receiving thiocyanates over a prolonged period in the treatment of hypertension.

Goiter produced by thiocyanates in many respects resembles a form of experimental goiter of great interest since it was first reported by Chesney, Clawson, and Webster in 1928, the so-called "cabbage goiter" or "cyanide goiter."

The cabbage goiters and the cyanide goiters, like those produced by thiocyanate, can be prevented by the simultaneous administration of iodine. The administration of iodine after the development of goiter in rabbits, however, resulted in the onset of symptoms of severe, sometimes fatal, hyperthyroidism.

Other important compounds recently found to have powerful goiter-producing effects fall mainly in two groups: (1) thiourea and various thiourea derivatives, and (2) sulfonamides and related substances.

Kennedy in 1942, reasoning that the goiter-producing effect of rapeseed might be due to a derivative of urea, injected allylthiourea into rats and found that it produced large goiters. Richter and Clisby in 1941 produced marked hyperplasia of the thyroid of rats by the administration of phenyl thiocarbamide. MacKenzie, MacKenzie, and McCollum in 1941 found that the administration of sulfaguanidine to rats resulted in enlargement of the thyroid, and in 1942 MacKenzie and MacKenzie produced goiters by administering thiourea, diethylthiourea, and allylthiourea as well as sulfaguanidine and other sulfonamide compounds. Astwood, Sullivan, Bissell, and Tyslowitz in 1943 produced enlarged thyroid glands in rats with both sulfonamide compounds and thiourea.

It is of interest that the experimental production of goiter by cyanides and thiocyanates has been prevented by the simultaneous administration of iodine, whereas the goitrogenic effect of thiourea, sulfanilamide, and related compounds cannot be prevented

by the administration of iodine, but can be prevented by the administration of desiccated thyroid or thyroxin. The administration of desiccated thyroid or thyroxin was also effective in reducing goiters after they had developed, regardless of whether they had followed the administration of cyanides, thiocyanates, thiourea, or sulfonamide compounds.

It has been assumed that the action of the various drugs which produce goiter is by means of an inhibition of, or interference with, the manufacture of the normal thyroid hormone. The resulting increase in activity of the thyroid-stimulating pituitary hormone brings about hyperplasia of the thyroid cells but does not bring about an increase in thyroid hormone, which is in fact reduced to subnormal levels. This inhibitory effect has been made use of clinically by the administration of thiourea or thiouracil to patients suffering from hyperthyroidism in the form of Graves' disease. In addition to the disappearance of toxic symptoms and a decrease in the basal metabolic rate, temporary increase in the size of the thyroid gland was observed in 3 of 9 patients treated with thiouracil by Williams and Bissell. Microscopically, the thyroid gland in cases of Graves' disease treated with thiouracil shows extreme hyperplasia with heightened epithelium, marked papillary infolding, and mitosis in the epithelial cells.

The authors said that in the thiocyanate goiter there is more cellular hypertrophy, and it is, therefore, more nearly comparable microscopically to an exophthalmic goiter, and that the thiouracil goiter is more of a cellular hyperplasia with mitosis very much in evidence, and is therefore more comparable to a carcinoma of the thyroid.

Mahorner, H.: Goiter in the Southern States. *Surgery*, 1944, 16: 764.

Goiter is more common in the southern states, than it had been generally believed. It is more common in southern Louisiana than in the northern part and more common along certain bayous.

The surgical mortality is higher in the South and the surgical mortality of goiter is definitely higher in the negro than in the white man. The author thinks that this is due not so much to the greater severity of the disease in the negro but to the poorer physical surroundings before and after operation, and hence the less prompt preoperative and postoperative response.

The author's material consisted of 101 patients who underwent 110 operations; of these, 7 were multiple-stage operations. Sixty-one patients were white and 40 were negroes. Fifty-five patients presented toxic goiters. There were 2 postoperative deaths, both of which might have been prevented by multiple-stage operations.

The author thinks that the negro should be added as a third group to the groups of the elderly and of the young who do not tolerate surgery well. Added cautiousness is necessary to determine the proper time and extent of the operation in the negro.

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